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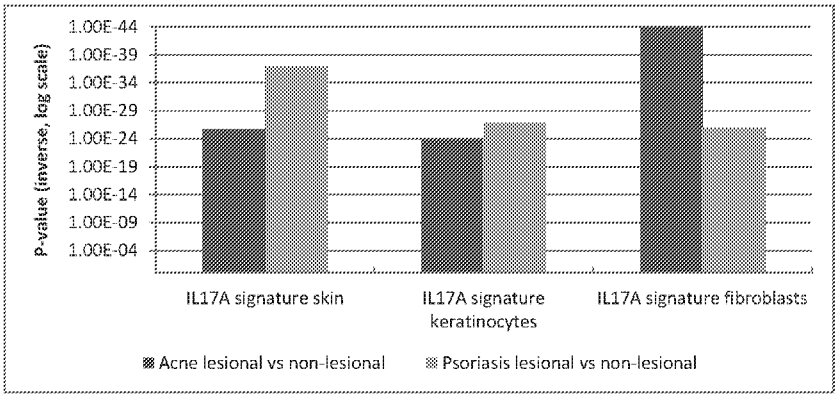
(54) **Title:** METHODS OF TREATING ACNE USING INTERLEUKIN-17 (IL-17) ANTAGONISTS

FIG 1.



(57) **Abstract:** The present disclosure relates to methods for treating acne, e.g., moderate to severe inflammatory acne, using IL-17 antagonists, e.g., secukinumab or CJM112. Also disclosed herein are uses of IL-17 antagonists, e.g., IL-17 antibodies, such as secukinumab or CJM112, for treating acne patients, as well as medicaments, dosing regimens, pharmaceutical formulations, dosage forms, and kits for use in the disclosed uses and methods.

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METHODS OF TREATING ACNE USING INTERLEUKIN-17 (IL-17) ANTAGONISTS

TECHNICAL FIELD

The present disclosure relates to methods for treating acne, e.g., moderate to severe inflammatory acne, using IL-17 antagonists, e.g., an IL-17 antibody or antigen-binding fragment thereof, such as secukinumab or CJM112.

BACKGROUND OF THE DISCLOSURE

Acne is one of the top 10 most prevalent diseases in the world, representing a high disease burden. (Hay et al. (2014) J Invest Dermatol. 134(6):1527-34). Moderate to severe acne patients' quality of life (QoL) is impacted in a manner similar to individuals having diabetes, epilepsy, asthma, back pain or arthritis. (Mallon et al. (1999) Br J Dermatol. 140(4):672-6; Cresce et al. (2014) J Drugs Dermatol. 13(6):692-7; Wen et al. (2015) Cell Biochem Biophys. 71(2):1083-8; Picardi et al. (2013) Clin Dermatol. 31(1):47-56). These individuals experience disfiguring inflamed lesions on the face and upper trunk and persistent facial scarring. As a result, individuals afflicted with acne display high levels of anxiety, major depressive disorders, and suicidial ideation. (Ramrakha et al. (2015) Br J Dermatol. doi: 10.1111/bjd.13786; Picardi et al., *supra*).

The current treatment for moderate to severe inflammatory acne is often a combination or association of several topical treatments (such as topical retinoids and antibacterials such as benzoylperoxide and antibiotics) with oral antibiotics, and/or hormonal treatment or retinoids, such as isotretinoin. (Gollnick et al. (2016) J Eur Acad Dermatol Venereol. doi: 10.1111/jdv.13675; Zaenglein et al. (2016) J Am Acad Dermatol. 74(5):945-973). However, oral antibiotic and hormonal treatments are often only moderately effective and isotretinoin, while effective in many cases, is associated with severe side effects, including teratogenicity, but also suicidal ideation, bone development issues, or increase of blood lipids, all sensitive side effects for a young adult and/or adolescent population. (Zaenglein et al., *supra*). The side effects

and the associated administrative hurdles due to pregnancy prevention programs in many countries preclude many patients to receive adequate effective treatment. Thus, there is a need for safe and effective treatments for acne, in particular moderate to severe acne and more particularly inflammatory acne.

SUMMARY OF THE DISCLOSURE

Kistowska et al. show that the mRNA expression levels of Th1 and Th17 effector cytokines, transcription factors, IL-17A, and chemokine receptors is strongly upregulated in acne lesions, and that *P. acnes* can promote mixed Th17/Th1 responses *in vitro* by inducing concomitant secretion of IL-17 and IFN-γ from CD4+ T cells. (Kistowska et al. (2015) J. Invest. Derm. 135:111-117; *see also* Jeremy et al (2003) J Invest Dermatol. 121(1):20-7 [CD4+ T cells involved in acne lesions]; Kelhala et al (2014) PLoS One. 9(8):e105238 [Th17 related cytokines are increased in acne lesions]). Increased IL-17A protein levels has also been identified in lesional versus non-lesional acne skin. (Kelhälä et al. (2014) PLoS ONE 8(8):1-18). Karadag et al. show that baseline serum levels of IL-17A are higher in patients with acne, and this decreases following treatment with isotretinoin, but the level following treatment remains higher than that of the non-acne control group (Karadag et al. (2012) Br. J. Dermatol. 167(2):433-5; *see also* Agak et al (2014) J Invest Dermatol. 134(2):366-73; Borovaya et al. (2014) Arch. Dermatol. Res. 306(8):689-700). Regardless, this research does not reveal whether IL-17A is a "passenger" or a "driver" in the development and persistence of acne, and, hence, whether antagonism of IL-17A would be effective for treating acne, e.g., moderate to severe inflammatory acne.

We have now determined that IL-17 antagonists, e.g., IL-17 antibodies, e.g., secukinumab and CJM112, can be used systemically to treat acne, e.g., moderate to severe inflammatory acne, and resolve the lesions accompanying the disorder.

Accordingly, disclosed herein are methods of treating acne, e.g., moderate to severe inflammatory acne, comprising administering an IL-17 antagonist (e.g., an anti-IL-17 antibody or antigen-binding fragment thereof) to a patient in need thereof.

In some embodiments of the disclosed uses, methods and kits, the IL-17 antibody or antigen-binding fragment thereof is: a) an IL-17 antibody or antigen-binding fragment thereof

that binds to an epitope of IL-17: i) between residues Arg 55 and Trp 67; ii) comprising Arg 55, Glu 57, and Trp 67; iii) comprising: Arg 55, Glu 57, Trp 67, Tyr 62, and Arg 101; iv) comprising Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, and Val 65; or v) comprising Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, Val 65, Val 22*, Leu 26, Asp 58, Glu 60, Pro 63, Pro 107, Phe 110, and Lys 114*, where amino acids marked with (*) designate a residue contributed by the second IL-17 subunit of the IL-17A homodimer, wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 1-10 pM (e.g., about 6 pM), and wherein the IL-17 antibody or antigen-binding fragment thereof has an *in vivo* half-life of about 2-4 weeks, e.g., about 3 weeks; or b) an IL-17 antibody or antigen-binding fragment thereof comprising: i) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:30; ii) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:22; iii) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:30 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:22; iv) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28; v) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20; vi) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27 and SEQ ID NO:29; vii) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21; viii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20; ix) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27, and SEQ ID NO:29 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21; x) a light chain comprising SEQ ID NO:23; xi) a heavy chain comprising SEQ ID NO:31; or xii) a light chain comprising SEQ ID NO:23 and a heavy chain comprising SEQ ID NO:31.

In some embodiments of the disclosed uses, methods and kits, the IL-17 antagonist is an IL-17 antibody or antigen-binding fragment thereof. In some embodiments of the disclosed

uses, methods and kits, the IL-17 antibody or antigen-binding fragment thereof is selected from the group consisting of: a) an IL-17 antibody or antigen-binding fragment thereof that binds to an epitope of IL-17 comprising Leu74, Tyr85, His86, Met87, Asn88, Val124, Thr125, Pro126, Ile127, Val128, His129; b) an IL-17 antibody or antigen-binding fragment thereof that binds to an epitope of IL-17 comprising Tyr43, Tyr44, Arg46, Ala79, Asp80; c) an IL-17 antibody or antigen-binding fragment thereof that binds to an epitope of an IL-17 homodimer having two mature IL-17 protein chains, said epitope comprising Leu74, Tyr85, His86, Met87, Asn88, Val124, Thr125, Pro126, Ile127, Val128, His129 on one chain and Tyr43, Tyr44, Arg46, Ala79, Asp80 on the other chain; d) an IL-17 antibody or antigen-binding fragment thereof that binds to an epitope of an IL-17 homodimer having two mature IL-17 protein chains, said epitope comprising Leu74, Tyr85, His86, Met87, Asn88, Val124, Thr125, Pro126, Ile127, Val128, His129 on one chain and Tyr43, Tyr44, Arg46, Ala79, Asp80 on the other chain, wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 100-200 pM (e.g., about 200 pM), and wherein the IL-17 antibody or antigen-binding fragment thereof has an *in vivo* half-life of about 3 to 5 weeks, e.g., about 4 weeks (e.g., about 23 to about 35 days [e.g., about 27 days]); and e) an IL-17 antibody or antigen-binding fragment thereof comprising: i) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:8; ii) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:10; iii) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:8 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:10; iv) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3; v) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6; vi) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13; vii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6; viii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 and an immunoglobulin V_L domain comprising the

hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6; ix) an immunoglobulin light chain comprising the amino acid sequence set forth as SEQ ID NO:14; x) an immunoglobulin heavy chain comprising the amino acid sequence set forth as SEQ ID NO:15; or xi) an immunoglobulin light chain comprising the amino acid sequence set forth as SEQ ID NO:14 and an immunoglobulin heavy chain comprising the amino acid sequence set forth as SEQ ID NO:15.

In some embodiments of the disclosed uses, methods and kits, the IL-17 antibody or antigen-binding fragment thereof is secukinumab (AIN457) or CJM112. Secukinumab and CJM112 are high-affinity recombinant, fully human monoclonal anti-human interleukin-17A antibodies of the IgG1/κ-class. Secukinumab and CJM112 bind to human IL-17A and neutralize the bioactivity of this cytokine.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 shows a comparison of skin and cell type derived IL17A signaling signatures with disease vs normal differentially expressed genes from a public Acne and Psoriasis study. P-values of a fisher exact T-test.

Figure 2 shows the influence of all-trans retinoic acid (ATRA) on the priming of Th17 T cells in Donor 1 (A) and Donor 2 (B).

Figure 3 shows the study design for the clinical trial set forth in Example 3.

Figure 4 shows results from the clinical trial set forth in Example 3 on facial inflammatory lesion count.

DETAILED DESCRIPTION OF THE DISCLOSURE

The invention relates to an IL-17 antagonist, e.g. an IL-17 binding molecule, e.g. an IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112, for use in treating or preventing acne, e.g. moderate to severe acne, e.g. moderate to severe inflammatory acne.

In another embodiment, the invention relates to a pharmaceutical composition comprising an IL-17 antagonist, e.g. an IL-17 binding molecule, e.g. an IL-17 antibody or antigen-binding

fragment thereof, e.g., secukinumab or CJM112, and at least one pharmaceutically acceptable excipient, for use in treating or preventing acne, e.g. moderate to severe acne, e.g. moderate to severe inflammatory acne.

In a further embodiment, the invention relates to a method of treating or preventing acne, e.g. moderate to severe acne, e.g. moderate to severe inflammatory acne. comprising administering a therapeutically effective amount of an IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112, to a patient in need thereof.

Further embodiments of the present invention are:

1. An IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne, e.g. moderate to severe acne, e.g. moderate to severe inflammatory acne.

2. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to embodiment 1, wherein the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of mature human IL-17: a) between residues Arg 55 and Trp 67; b) comprising residues Arg 55, Glu 57, and Trp 67; c) comprising residues Arg 55, Glu 57, Trp 67, Tyr 62, and Arg 101; d) comprising residues Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, and Val 65; or e) comprising residues Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, Val 65, Val 22*, Leu 26, Asp 58, Glu 60, Pro 63, Pro 107, Phe 110, and Lys 114*, where amino acids marked with (*) designate a residue contributed by the second IL-17 subunit of the IL-17A homodimer, and further wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 1-10 pM and an in vivo half-life of about 2-4 weeks, e.g., about 3 weeks.

3. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to embodiment 1, wherein the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of a human IL-17 homodimer having two mature human IL-17 protein chains, said epitope comprising residues Leu74, Tyr85, His86, Met87, Asn88, Val124, Thr125, Pro126, Ile127, Val128, His129 on one chain and Tyr43, Tyr44, Arg46, Ala79, Asp80

on the other chain, wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 100-200 pM, and wherein the IL-17 antibody or antigen-binding fragment thereof has an *in vivo* half-life of about 3-5 weeks, e.g., about 4 weeks.

4. An IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to embodiment 1 or 2, wherein the IL-17 antibody or antigen-binding fragment thereof comprises:

i) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:30; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

ii) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:22; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

iii) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:30 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:22; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

iv) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

v) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

vi) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27 and SEQ ID NO:29; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

vii) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

viii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

ix) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27, and SEQ ID NO:29 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

x) a light chain comprising SEQ ID NO:23; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

xi) a heavy chain comprising SEQ ID NO:31; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

xii) a light chain comprising SEQ ID NO:23 and a heavy chain comprising SEQ ID NO:31; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto.

5. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to embodiment 1 or 3, wherein the IL-17 antibody or antigen-binding fragment thereof comprises:

i) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:8; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

ii) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:10; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

iii) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:8 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:10; or an amino acid sequence having at least about 95%, 98% or 99% overall

sequence identity thereto;

iv) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

v) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

vi) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

vii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

viii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6 ; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

ix) an immunoglobulin light chain comprising the amino acid sequence set forth as SEQ ID NO:14; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

x) an immunoglobulin heavy chain comprising the amino acid sequence set forth as SEQ ID NO:15; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto; or

xi) an immunoglobulin light chain comprising the amino acid sequence set forth as SEQ ID NO:14 and an immunoglobulin heavy chain comprising the amino acid sequence set forth as SEQ ID NO:15; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto.

6. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any one of the embodiments above, wherein the IL-17 antibody or antigen-binding fragment thereof is a human antibody.

7. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any of the above embodiments, wherein the IL-17 antibody or antigen-binding fragment thereof is administered for up to 24 weeks.

8. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any the above embodiments, wherein the IL-17 antibody or antigen-binding fragment thereof is administered subcutaneously at an unit dose of about 75 mg to about 600 mg, about 75mg to about 450mg, or about 75 mg to about 300 mg, quarterly, monthly or weekly, e.g. monthly.

9. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to embodiment 8, wherein the IL-17 antibody or antigen-binding fragment thereof is administered subcutaneously at an unit dose of about 75mg, about 150mg, about 300mg, about 350mg, about 400mg, about 450mg, about 500mg, about 550mg, or about 600mg. The unit dose is administered quarterly, monthly or weekly, e.g. monthly or weekly, e.g. monthly.

10. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any of the above embodiments, wherein the IL-17 antibody or antigen-binding fragment thereof is administered by subcutaneous injection at an unit dose of about 75 mg to about 600 mg, preferably about 75 mg to about 300 mg, preferably about 300 mg to about 450 mg, wherein said administering is not preceded by administering said IL-17 antibody or antigen-binding fragment in a loading regimen. The unit dose is administered quarterly, monthly or weekly, e.g. monthly or weekly, e.g. monthly.

11. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any of the above embodiments, wherein the IL-17 antibody or antigen-binding fragment thereof is administered by subcutaneous injection, at a loading dose of about 75 mg to about 600 mg, preferably about 75 mg to about 300 mg, preferably about 300 mg to about 450 mg. The loading dose is administered e.g. weekly.

12. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to embodiment 11, wherein the loading dose is administered during 1 to 8 weeks, preferably during 4 or 5 weeks.

13. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to embodiment 12, wherein the IL-17 antibody or antigen-binding fragment thereof is administered subcutaneously at a dosing of about 75 mg to about 600 mg, preferably about 75 mg to about 300 mg or about 300 mg to about 450 mg, weekly during week 0, 1, 2, 3, and 4, and then monthly thereafter.

14. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any one of embodiments 1 to 6, wherein the IL-17 antibody or antigen-binding fragment thereof is administered as a single dose. This single dose can be administered subcutaneously and be of about 150 mg to about 600 mg, e.g. of about 75 mg to about 300 mg or about 300 mg to about 450 mg.

15. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to embodiment 4 or any one of embodiments 6 to 14, wherein the IL-17 antibody or antigen-binding fragment thereof is CJM112, a functional derivative or biosimilar thereof, e.g. CJM112.

16. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to embodiment 15, wherein the IL-17 antibody or antigen-binding fragment thereof is CJM112, a functional derivative or biosimilar thereof, e.g. CJM112, and the IL-17

antibody or antigen-binding fragment thereof is administered subcutaneously at an unit dose of about 75mg to about 600mg, e.g. about 150 mg to about 600 mg, e.g. about 150 mg to about 450 mg, e.g. about 300 mg to about 450 mg. Such administrations are for example weekly or monthly; they can be weekly for several weeks (e.g 1 to 8 weeks, e.g. 4 or 5 weeks) and then monthly.

17. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any one of embodiments 5 to 14, wherein the IL-17 antibody or antigen-binding fragment thereof is secukinumab, a functional derivative or biosimilar thereof, e.g. secukinumab.

18. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing moderate to severe acne according to embodiment 17, comprising administering the patient a single dose of about 75mg to about 600mg, e.g. about 150 mg to about 600 mg, e.g. about 150 mg to about 450 mg, e.g. about 300 mg to about 450 mg, of secukinumab, a functional derivative or biosimilar thereof, e.g. Secukinumab, by subcutaneous injection.

19. An IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing moderate to severe acne, that is secukinumab, a functional derivative or biosimilar thereof, e.g., secukinumab, wherein the IL-17 antibody or antigen-binding fragment thereof is administered subcutaneously at a dosing of about 75 mg to about 600 mg, preferably about 75 mg to about 300 mg or about 300 mg to about 450 mg, weekly, during 1 to 8 weeks and then monthly thereafter.

20. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing moderate to severe acne according to embodiment 19, wherein secukinumab, a functional derivative or biosimilar thereof, e.g. secukinumab, is administered during week 0, 1, 2, 3 and 4, and then monthly thereafter.

21. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to embodiment 15 or 17, wherein the IL-17 antibody or antigen-binding fragment

thereof is administered intravenously at a dose of about 10mg/kg, e.g. monthly or weekly.

22. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any one of the embodiments above, wherein the patient was previously treated for acne with a topical anti-acne treatment, an oral/systemic anti-acne treatment, a systemic or lesional injected anti-acne treatment, or surgical, physical, light or laser therapy.

22. A method of treating acne, comprising administering a therapeutically effective amount of an IL-17 antibody or antigen-binding fragment thereof to a patient in need thereof, wherein the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of mature human IL-17: a) between residues Arg 55 and Trp 67; b) comprising residues Arg 55, Glu 57, and Trp 67; c) comprising residues Arg 55, Glu 57, Trp 67, Tyr 62, and Arg 101; d) comprising residues Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, and Val 65; or e) comprising residues Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, Val 65, Val 22*, Leu 26, Asp 58, Glu 60, Pro 63, Pro 107, Phe 110, and Lys 114*, where amino acids marked with (*) designate a residue contributed by the second IL-17 subunit of the IL-17A homodimer, and further wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 1-10 pM and an in vivo half-life of about 2-4 weeks, e.g., about 3 weeks.

23. A method of treating acne, comprising administering a therapeutically effective amount of an IL-17 antibody or antigen-binding fragment thereof to a patient in need thereof, wherein the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of a human IL-17 homodimer having two mature human IL-17 protein chains, said epitope comprising residues Leu74, Tyr85, His86, Met87, Asn88, Val124, Thr125, Pro126, Ile127, Val128, His129 on one chain and Tyr43, Tyr44, Arg46, Ala79, Asp80 on the other chain, wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 100-200 pM, and wherein the IL-17 antibody or antigen-binding fragment thereof has an *in vivo* half-life of about 3-5 weeks, e.g., about 4 weeks.

24. The method according to embodiments 22 and 23, wherein the patient has moderate to severe inflammatory acne.

25. The method according to any of the embodiments 22 to 24, wherein the patient is treated for up to 24 weeks with the IL-17 antibody or antigen-binding fragment thereof.

26. The method according to any of the embodiments 22 to 25, wherein the patient was previously treated for acne with a topical anti-acne treatment, an oral/systemic anti-acne treatment, a systemic or lesional injected anti-acne treatment, or surgical, physical, light or laser therapy.

27. The method according to any of the embodiments 22 to 26, comprising administering the patient a single dose of about 150 mg to about 600 mg of the IL-17 antibody or antigen-binding fragment thereof by subcutaneous injection.

28. The method according to any of the embodiments 22 to 27, comprising quarterly or monthly administering the patient about 75 mg to about 600 mg, preferably about 75 mg to about 300 mg or about 300 mg to about 450 mg, of the IL-17 antibody or antigen-binding fragment thereof by subcutaneous injection.

29. The method according to embodiment 28, comprising monthly administering the patient about 75 mg of the IL-17 antibody or antigen-binding fragment thereof by subcutaneous injection.

30. The method according to embodiment 28, comprising monthly administering the patient about 300 mg of the IL-17 antibody or antigen-binding fragment thereof by subcutaneous injection.

30bis. The method according to embodiment 28, comprising monthly administering the patient about 450 mg of the IL-17 antibody or antigen-binding fragment thereof by subcutaneous injection.

31. The method according to embodiment 22, wherein the IL-17 antibody or antigen-binding fragment thereof comprises:

i) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:30;

ii) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:22;

iii) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:30 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:22;

iv) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28;

v) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20;

vi) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27 and SEQ ID NO:29;

vii) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21;

viii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20;

ix) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27, and SEQ ID NO:29 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21;

x) a light chain comprising SEQ ID NO:23; xi) a heavy chain comprising SEQ ID NO:31; or

xii) a light chain comprising SEQ ID NO:23 and a heavy chain comprising SEQ ID NO:31.

32. The method according to embodiment 31, wherein the IL-17 antibody or antigen-binding fragment thereof is a human antibody.

33. The method according to embodiment 32, wherein the IL-17 antibody or antigen-binding fragment thereof is CJM112.

34. A method of treating a patient having acne, e.g. moderate to severe inflammatory acne, comprising monthly administering the patient about 75 mg to about 600 mg, about 75mg to about 600mg, e.g. about 150 mg to about 600 mg, e.g. about 150 mg to about 450 mg, e.g. about 300 mg to about 450 mg, of CJM112 (or a functional derivative or biosimilar thereof, preferably CJM112) by subcutaneous injection, wherein said monthly administering is optionally not preceded by administering the patient CJM112 in a loading regimen.

34.1 A method of treating a patient having acne, e.g. moderate to severe inflammatory acne, comprising monthly administering the patient about about 75 mg to about 300 mg or about 300 mg to about 450 mg, of CJM112 (or a functional derivative or biosimilar thereof, preferably CJM112) by subcutaneous injection, wherein said monthly administering is not preceded by administering the patient CJM112 in a loading regimen.

35. A method of treating a patient having acne, e.g. moderate to severe acne, e.g. moderate to severe inflammatory acne, comprising administering the patient a single dose of about 75 mg to about 600 mg, e.g about 75 mg to about 300 mg, e.g. about 150 mg to about 600 mg, e.g. about 150 mg to about 450 mg, e.g. about 300 mg to about 450 mg, of CJM112 (or a functional derivative or biosimilar thereof, preferably CJM112) by subcutaneous injection.

36. The method according to embodiment 23, wherein the IL-17 antibody or antigen-binding fragment thereof comprises:

i) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:8;

ii) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:10;

iii) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:8 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:10;

iv) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3;

v) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6;

vi) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13;

vii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6;

viii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6;

ix) an immunoglobulin light chain comprising the amino acid sequence set forth as SEQ ID NO:14;

x) an immunoglobulin heavy chain comprising the amino acid sequence set forth as SEQ ID NO:15; or

xi) an immunoglobulin light chain comprising the amino acid sequence set forth as SEQ ID NO:14 and an immunoglobulin heavy chain comprising the amino acid sequence set forth as SEQ ID NO:15.

37. The method according to embodiment 36, wherein the IL-17 antibody or antigen-binding fragment thereof is a human antibody.

38. The method according to embodiment 37, wherein the IL-17 antibody or antigen-binding fragment thereof is secukinumab, a functional derivative or biosimilar thereof, e.g. secukinumab.

39. A method of treating a patient having acne, e.g moderate to severe acne, e.g. moderate to severe inflammatory acne, comprising administering the patient a single dose of about 75 mg to about 600 mg, e.g. about 150 mg to about 600 mg, e.g. about 150 mg to about 450 mg, e.g. about 300 mg to about 450 mg, e.g. about 75 mg to about 300 mg of secukinumab (or a functional derivative or biosimilar thereof, e.g. Secukinumab) by subcutaneous injection.

40. A method of treating a patient having acne, e.g. moderate to severe acne, e.g. moderate to severe inflammatory acne, comprising subcutaneously administering to the patient about 75 mg to about 600 mg, e.g. about 150 mg to about 600 mg, e.g. about 150 mg to about 450 mg, e.g. about 300 mg to about 450 mg, e.g. about 75 mg to about 300 mg, of Secukinumab (or a functional derivative or biosimilar thereof, e.g. Secukinumab), weekly during week 0, 1, 2, 3, and 4, and then monthly thereafter.

41. A method of treating a patient having acne, e.g. moderate to severe acne, e.g. moderate to severe inflammatory acne, comprising intraveneously administering to the patient about 10mg/kg.

Additional embodiments are described below:

A1. Use of an IL-17 antibody or antigen-binding fragment thereof in the preparation of a medicament for treating or preventing acne, e.g. moderate to severe acne, e.g. moderate to severe inflammatory acne.

A2. Use according to embodiment A1, wherein the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of mature human IL-17: a) between residues Arg 55 and Trp 67; b) comprising residues Arg 55, Glu 57, and Trp 67; c) comprising residues Arg 55, Glu 57,

Trp 67, Tyr 62, and Arg 101; d) comprising residues Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, and Val 65; or e) comprising residues Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, Val 65, Val 22*, Leu 26, Asp 58, Glu 60, Pro 63, Pro 107, Phe 110, and Lys 114*, where amino acids marked with (*) designate a residue contributed by the second IL-17 subunit of the IL-17A homodimer, and further wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 1-10 pM and an in vivo half-life of about 2-4 weeks, e.g., about 3 weeks.

A3. Use according to embodiment A1, wherein the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of a human IL-17 homodimer having two mature human IL-17 protein chains, said epitope comprising residues Leu74, Tyr85, His86, Met87, Asn88, Val124, Thr125, Pro126, Ile127, Val128, His129 on one chain and Tyr43, Tyr44, Arg46, Ala79, Asp80 on the other chain, wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 100-200 pM, and wherein the IL-17 antibody or antigen-binding fragment thereof has an *in vivo* half-life of about 3-5 weeks, e.g., about 4 weeks.

A4. Use according to embodiment A1 or A2, wherein the IL-17 antibody or antigen-binding fragment thereof comprises:

i) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:30; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

ii) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:22; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

iii) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:30 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:22; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

iv) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

v) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

vi) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27 and SEQ ID NO:29; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

vii) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

viii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

ix) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27, and SEQ ID NO:29 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

x) a light chain comprising SEQ ID NO:23; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

xi) a heavy chain comprising SEQ ID NO:31; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

xii) a light chain comprising SEQ ID NO:23 and a heavy chain comprising SEQ ID NO:31; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto.

A5. Use according to embodiment A1 or A3, wherein the IL-17 antibody or antigen-binding fragment thereof comprises:

i) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:8; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

ii) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:10; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

iii) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:8 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:10; or an amino acid sequence having at least about 95%, 98% or 99% overall sequence identity thereto;

iv) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

v) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

vi) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

vii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

viii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6 ; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence

identity thereto;

ix) an immunoglobulin light chain comprising the amino acid sequence set forth as SEQ ID NO:14; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto;

x) an immunoglobulin heavy chain comprising the amino acid sequence set forth as SEQ ID NO:15; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto; or

xi) an immunoglobulin light chain comprising the amino acid sequence set forth as SEQ ID NO:14 and an immunoglobulin heavy chain comprising the amino acid sequence set forth as SEQ ID NO:15; or an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity thereto.

A6. Use according to any one of the embodiments A1 to A5, wherein the IL-17 antibody or antigen-binding fragment thereof is a human antibody.

A7. Use according to any of the embodiments A1 to A6, wherein the IL-17 antibody or antigen-binding fragment thereof is administered for up to 24 weeks.

A8. Use according to any the above embodiments A1 to A7, wherein the IL-17 antibody or antigen-binding fragment thereof is administered quarterly or monthly, e.g. subcutaneously at a dosing of about 75 mg to about 600 mg, about 75mg to about 450mg, or about 75 mg to about 300 mg.

A9. Use according to embodiment A8, wherein the IL-17 antibody or antigen-binding fragment thereof is administered monthly, by subcutaneous injection, at a dosing of about 75 mg, about 150mg, about 300mg, about 450mg or about 600mg.

A10. Use according to any of the above embodiments A1 to A9, wherein the IL-17 antibody or antigen-binding fragment thereof is administered by subcutaneous injection at a dosing of about 75 mg to about 600 mg, preferably about 75 mg to about 300 mg, wherein said administering is

not preceded by administering said IL-17 antibody or antigen-binding fragment in a loading regimen.

A11. Use according to any of the above embodiments A1 to A10, wherein the IL-17 antibody or antigen-binding fragment thereof is administered by subcutaneous injection, weekly, at a loading dose of about 75 mg to about 600 mg, preferably about 75 mg to about 300 mg.

A12. Use according to embodiment A11, wherein the loading dose is administered during 1 to 8 weeks, preferably during 4 or 5 weeks.

A13. Use according to embodiment A12, wherein the IL-17 antibody or antigen-binding fragment thereof is administered subcutaneously at a dosing of about 75 mg to about 600 mg, preferably about 75 mg – about 300 mg, weekly during week 0, 1, 2, 3, and 4, and then monthly thereafter.

A14. Use according to any one of embodiments A1 to A6, wherein the IL-17 antibody or antigen-binding fragment thereof is administered as a single dose, e.g. of about 150 mg to about 600 mg subcutaneously.

A15. Use according to embodiment A4 or any one of embodiments 6 to 14 , wherein the IL-17 antibody or antigen-binding fragment thereof is CJM112, a functional derivative or biosimilar thereof, e.g. CJM112.

A16. Use according to embodiment A15, wherein the IL-17 antibody or antigen-binding fragment thereof is CJM112, a functional derivative or biosimilar thereof, e.g. CJM112, and the IL-17 antibody or antigen-binding fragment thereof is administered subcutaneously at a dose of about 75mg to about 600mg, e.g. about 150 mg to about 600 mg, e.g. about 150 mg to about 450 mg, e.g. about 300 mg to about 450 mg. Such administrations are for example weekly or monthly; they can be weekly for several weeks (e.g 1 to 8 weeks, e.g. 4 or 5 weeks) and then monthly.

A17. Use according to any one of embodiments A5 to A14, wherein the IL-17 antibody or antigen-binding fragment thereof is secukinumab, a functional derivative or biosimilar thereof, e.g. secukinumab.

A18. Use according to embodiment A17, comprising administering the patient a single dose of about 75mg to about 600mg, e.g. about 150 mg to about 600 mg, e.g. about 150 mg to about 450 mg, e.g. about 300 mg to about 450 mg, of secukinumab, a functional derivative or biosimilar thereof, e.g. Secukinumab, by subcutaneous injection.

A19. The use of an IL-17 antibody or antigen-binding fragment thereof in the preparation of a medicament for treating or preventing moderate to severe acne, that is secukinumab, a functional derivative or biosimilar thereof, e.g., secukinumab, wherein the IL-17 antibody or antigen-binding fragment thereof is administered subcutaneously at a dosing of about 75 mg to about 600 mg, preferably about 75 mg to about 300 mg, weekly, during 1 to 8 weeks and then monthly thereafter.

A20. The use of an IL-17 antibody or antigen-binding fragment thereof in the preparation of a medicament for treating or preventing moderate to severe acne according to embodiment A19, wherein secukinumab, a functional derivative or biosimilar thereof, e.g. secukinumab, is administered during week 0, 1, 2, 3 and 4, and then monthly thereafter.

A21. Use according to any one of the embodiments A1 to A20, wherein the patient was previously treated for acne with a topical anti-acne treatment, an oral/systemic anti-acne treatment, a systemic or lesional injected anti-acne treatment, or surgical, physical, light or laser therapy.

Furthermore embodiments are described below:

B1. Use of a pharmaceutical composition comprising of an IL-17 antibody or antigen-binding fragment thereof, and one or more pharmaceutically acceptable carriers, in the manufacture medicament for treating or preventing acne, according to any of the above embodiments (e.g. A1 to A21).

As used herein, IL-17 refers to interleukin-17A (IL-17A).

The term "comprising" encompasses "including" as well as "consisting," e.g., a composition "comprising" X may consist exclusively of X or may include something additional, e.g., X + Y.

As used herein, the phrase "TNF-alpha antagonist" refers to small molecules and biological molecules capable of inhibiting, reducing and/or blocking TNF-alpha signal, transduction, and/or activity. Examples of TNF-alpha antagonists include Enbrel® (etanercept), Humira® (adalimumab), Remicade® (infliximab) and Simponi® (golimumab).

The term "about" in relation to a numerical value x means, for example, +/-10%. When used in front of a numerical range or list of numbers, the term "about" applies to each number in the series, e.g., the phrase "about 1-5" should be interpreted as "about 1 – about 5", or, e.g., the phrase "about 1, 2, 3, 4" should be interpreted as "about 1, about 2, about 3, about 4, etc."

The word "substantially" does not exclude "completely," e.g., a composition which is "substantially free" from Y may be completely free from Y. Where necessary, the word "substantially" may be omitted from the definition of the disclosure.

The term "antibody" as referred to herein includes naturally-occurring and whole antibodies. A naturally-occurring "antibody" is a glycoprotein comprising at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds. Each heavy chain is comprised of a heavy chain variable region (abbreviated herein as V_H) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, CH1, CH2 and CH3. Each light chain is comprised of a light chain variable region (abbreviated herein as V_L) and a light chain constant region. The light chain constant region is comprised of one domain, CL. The V_H and V_L regions can be further subdivided into regions of hypervariability, termed hypervariable regions or complementarity determining regions (CDR), interspersed with regions

that are more conserved, termed framework regions (FR). Each V_H and V_L is composed of three CDRs and four FRs arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The variable regions of the heavy and light chains contain a binding domain that interacts with an antigen. The constant regions of the antibodies may mediate the binding of the immunoglobulin to host tissues or factors, including various cells of the immune system (e.g., effector cells) and the first component (C1q) of the classical complement system. Exemplary antibodies include secukinumab (**Table 1**), CJM112 (**Table 2**) and ixekizumab (U.S. Patent No. 7,838,638).

The term "antigen-binding fragment" of an antibody, as used herein, refers to fragments of an antibody that retain the ability to specifically bind to an antigen (e.g., IL-17). It has been shown that the antigen-binding function of an antibody can be performed by fragments of a full-length antibody. Examples of binding fragments encompassed within the term "antigen-binding portion" of an antibody include a Fab fragment, a monovalent fragment consisting of the V_L, V_H, CL and CH1 domains; a F(ab)2 fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; a Fd fragment consisting of the V_H and CH1 domains; a Fv fragment consisting of the V_L and V_H domains of a single arm of an antibody; a dAb fragment (Ward et al., 1989 Nature 341:544-546), which consists of a V_H domain; and an isolated CDR. Exemplary antigen-binding sites include the CDRs of secukinumab as set forth in SEQ ID NOs: 1-6 and 11-13 (**Table 1**), preferably the heavy chain CDR3. Exemplary antigen-binding sites include the CDRs of CJM112 as set forth in SEQ ID NOs: 16-21 and 24-30 (**Table 2**), preferably the heavy chain CDR3. Furthermore, although the two domains of the Fv fragment, V_L and V_H, are coded for by separate genes, they can be joined, using recombinant methods, by a synthetic linker that enables them to be made as a single protein chain in which the V_L and V_H regions pair to form monovalent molecules (known as single chain Fv (scFv); see, e.g., Bird et al., 1988 Science 242:423-426; and Huston et al., 1988 Proc. Natl. Acad. Sci. 85:5879-5883). Such single chain antibodies are also intended to be encompassed within the term "antibody". Single chain antibodies and antigen-binding portions are obtained using conventional techniques known to those of skill in the art.

An "isolated antibody", as used herein, refers to an antibody that is substantially free of other antibodies having different antigenic specificities (e.g., an isolated antibody that

specifically binds IL-17 is substantially free of antibodies that specifically bind antigens other than IL-17). The term "monoclonal antibody" or "monoclonal antibody composition" as used herein refer to a preparation of antibody molecules of single molecular composition. The term "human antibody", as used herein, is intended to include antibodies having variable regions in which both the framework and CDR regions are derived from sequences of human origin. A "human antibody" need not be produced by a human, human tissue or human cell. The human antibodies of the disclosure may include amino acid residues not encoded by human sequences (e.g., mutations introduced by random or site-specific mutagenesis *in vitro*, by N-nucleotide addition at junctions *in vivo* during recombination of antibody genes, or by somatic mutation *in vivo*). In some embodiments of the disclosed processes and compositions, the IL-17 antibody is a human antibody, an isolated antibody, and/or a monoclonal antibody.

The term "IL-17" refers to IL-17A, formerly known as CTLA8, and includes wild-type IL-17A from various species (e.g., human, mouse, and monkey), polymorphic variants of IL-17A, and functional equivalents of IL-17A. Functional equivalents of IL-17A according to the present disclosure preferably have at least about 65%, 75%, 85%, 95%, 96%, 97%, 98%, or even 99% overall sequence identity with a wild-type IL-17A (e.g., human IL-17A), and substantially retain the ability to induce IL-6 production by human dermal fibroblasts.

The term "K_D" is intended to refer to the dissociation rate of a particular antibody-antigen interaction. The term "K_D", as used herein, is intended to refer to the dissociation constant, which is obtained from the ratio of k_{off} to k_{on} (i.e., k_{off} / k_{on}) and is expressed as a molar concentration (M). K_D values for antibodies can be determined using methods well established in the art. A method for determining the K_D of an antibody is by using surface plasmon resonance, or using a biosensor system such as a Biacore® system. In some embodiments, the IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112, binds human IL-17 with a K_D of about 1-250 pM, preferably about 1-10 pM (e.g., about 6 pM) or about 100-200 pM (e.g., about 200 pM).

The term "affinity" refers to the strength of interaction between antibody and antigen at single antigenic sites. Within each antigenic site, the variable region of the antibody "arm" interacts through weak non-covalent forces with antigen at numerous sites; the more interactions, the stronger the affinity. Standard assays to evaluate the binding affinity of the antibodies

toward IL-17 of various species are known in the art, including for example, ELISAs, western blots and RIAs. The binding kinetics (e.g., binding affinity) of the antibodies also can be assessed by standard assays known in the art, such as by Biacore analysis.

An antibody that "inhibits" one or more of these IL-17 functional properties (e.g., biochemical, immunochemical, cellular, physiological or other biological activities, or the like) as determined according to methodologies known to the art and described herein, will be understood to relate to a statistically significant decrease in the particular activity relative to that seen in the absence of the antibody (or when a control antibody of irrelevant specificity is present). An antibody that inhibits IL-17 activity affects a statistically significant decrease, e.g., by at least about 10% of the measured parameter, by at least 50%, 80% or 90%, and in certain embodiments of the disclosed methods and compositions, the IL-17 antibody used may inhibit greater than 95%, 98% or 99% of IL-17 functional activity.

"Inhibit IL-6" as used herein refers to the ability of an IL-17 antibody or antigen-binding fragment thereof (e.g., secukinumab or CJM112) to decrease IL-6 production from primary human dermal fibroblasts. The production of IL-6 in primary human (dermal) fibroblasts is dependent on IL-17 (Hwang et al., (2004) Arthritis Res Ther; 6:R120-128). In short, human dermal fibroblasts are stimulated with recombinant IL-17 in the presence of various concentrations of an IL-17 binding molecule or human IL-17 receptor with Fc part. The chimeric anti-CD25 antibody Simulect® (basiliximab) may be conveniently used as a negative control. Supernatant is taken after 16 h stimulation and assayed for IL-6 by ELISA. An IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112, typically has an IC_{50} for inhibition of IL-6 production (in the presence 1 nM human IL-17) of about 50 nM or less (e.g., from about 0.01 to about 50 nM) when tested as above, i.e., said inhibitory activity being measured on IL-6 production induced by hu-IL-17 in human dermal fibroblasts. In some embodiments of the disclosed methods and compositions, IL-17 antibodies or antigen-binding fragments thereof, e.g., secukinumab or CJM112, and functional derivatives thereof have an IC_{50} for inhibition of IL-6 production as defined above of about 20 nM or less, more preferably of about 10 nM or less, more preferably of about 5 nM or less, more preferably of about 2 nM or less, more preferably of about 1 nM or less.

The term "derivative", unless otherwise indicated, is used to define amino acid sequence variants, and covalent modifications (e.g., pegylation, deamidation, hydroxylation, phosphorylation, methylation, etc.) of an IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112, according to the present disclosure, e.g., of a specified sequence (e.g., a variable domain). A "functional derivative" includes a molecule having a qualitative biological activity in common with the disclosed IL-17 antibodies. A functional derivative includes fragments and peptide analogs of an IL-17 antibody as disclosed herein. Fragments comprise regions within the sequence of a polypeptide according to the present disclosure, e.g., of a specified sequence. Functional derivatives of the IL-17 antibodies disclosed herein (e.g., functional derivatives of secukinumab or CJM112) preferably comprise V_H and/or V_L domains that have at least about 65%, 75%, 85%, 95%, 96%, 97%, 98%, or even 99% overall sequence identity with the V_H and/or V_L sequences of the IL-17 antibodies and antigen-binding fragments thereof disclosed herein, and substantially retain the ability to bind human IL-17 or, e.g., inhibit IL-6 production of IL-17 induced human dermal fibroblasts.

The phrase "substantially identical" means that the relevant amino acid or nucleotide sequence (e.g., V_H or V_L domain) will be identical to or have insubstantial differences (e.g., through conserved amino acid substitutions) in comparison to a particular reference sequence. Insubstantial differences include minor amino acid changes, such as 1 or 2 substitutions in a 5 amino acid sequence of a specified region (e.g., V_H or V_L domain). In the case of antibodies, the second antibody has the same specificity and has at least 50% of the affinity of the same. Sequences substantially identical (e.g., at least about 85% sequence identity) to the sequences disclosed herein are also part of this application. In some embodiments, the sequence identity of a derivative IL-17 antibody (e.g., a derivative of secukinumab or CJM112, e.g., a secukinumab or CJM112 biosimilar antibody) can be about 90% or greater, e.g., 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or higher relative to the disclosed sequences.

"Identity" with respect to a native polypeptide and its functional derivative is defined herein as the percentage of amino acid residues in the candidate sequence that are identical with the residues of a corresponding native polypeptide, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent identity, and not considering any conservative substitutions as part of the sequence identity. Neither N- or C-terminal extensions

nor insertions shall be construed as reducing identity. Methods and computer programs for the alignment are well known. The percent identity can be determined by standard alignment algorithms, for example, the Basic Local Alignment Search Tool (BLAST) described by Altshul et al. ((1990) J. Mol. Biol., 215: 403 410); the algorithm of Needleman et al. ((1970) J. Mol. Biol., 48: 444 453); or the algorithm of Meyers et al. ((1988) Comput. Appl. Biosci., 4: 11 17). A set of parameters may be the Blosum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5. The percent identity between two amino acid or nucleotide sequences can also be determined using the algorithm of E. Meyers and W. Miller ((1989) CABIOS, 4:11-17) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

"Amino acid(s)" refer to all naturally occurring L-α-amino acids, e.g., and include D-amino acids. The phrase "amino acid sequence variant" refers to molecules with some differences in their amino acid sequences as compared to the sequences according to the present disclosure. Amino acid sequence variants of an antibody according to the present disclosure, e.g., of a specified sequence, still have the ability to bind the human IL-17 or, e.g., inhibit IL-6 production of IL-17 induced human dermal fibroblasts. Amino acid sequence variants include substitutional variants (those that have at least one amino acid residue removed and a different amino acid inserted in its place at the same position in a polypeptide according to the present disclosure), insertional variants (those with one or more amino acids inserted immediately adjacent to an amino acid at a particular position in a polypeptide according to the present disclosure) and deletional variants (those with one or more amino acids removed in a polypeptide according to the present disclosure).

The term "pharmaceutically acceptable" means a nontoxic material that does not interfere with the effectiveness of the biological activity of the active ingredient(s).

The term "administering" in relation to a compound, e.g., an IL-17 binding molecule or another agent, is used to refer to delivery of that compound to a patient by any route.

As used herein, a "therapeutically effective amount" refers to an amount of an IL-17 antagonist, e.g., IL-17 binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof) that is effective, upon single or multiple dose

administration to a patient (such as a human) for treating, preventing, preventing the onset of, curing, delaying, reducing the severity of, ameliorating at least one symptom of a disorder or recurring disorder, or prolonging the survival of the patient beyond that expected in the absence of such treatment. When applied to an individual active ingredient (e.g., an IL-17 antagonist, e.g., secukinumab or CJM112) administered alone, the term refers to that ingredient alone. When applied to a combination, the term refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

The term "treatment" or "treat" refer to curative or disease modifying treatment, including treatment of a patient at risk of contracting the disease or suspected to have contracted the disease as well as patients who are ill or have been diagnosed as suffering from a disease or medical condition, and includes suppression of clinical relapse. The treatment may be administered to a patient having a medical disorder or who ultimately may acquire the disorder, in order to prevent, cure, delay the onset of, reduce the severity of, or ameliorate one or more symptoms of a disorder or recurring disorder, or in order to prolong the survival of a patient beyond that expected absent such treatment.

The term "prevent" or "preventing" refer to prophylactic or preventative treatment; it is concerned about delaying the onset of, or preventing the onset of the disease, disorders and/or symptoms associated thereto.

As used herein, "selecting" and "selected" in reference to a patient is used to mean that a particular patient is specifically chosen from a larger group of patients on the basis of (due to) the particular patient having a predetermined criteria. Similarly, "selectively treating" refers to providing treatment to a patient having a particular disease, where that patient is specifically chosen from a larger group of patients on the basis of the particular patient having a predetermined criterion. Similarly, "selectively administering" refers to administering a drug to a patient that is specifically chosen from a larger group of patients on the basis of (due to) the particular patient having a predetermined criterion. By selecting, selectively treating and selectively administering, it is meant that a patient is delivered a personalized therapy based on the patient's personal history (e.g., prior therapeutic interventions, e.g., prior treatment with biologics), biology (e.g., particular genetic markers), and/or manifestation (e.g., not fulfilling

particular diagnostic criteria), rather than being delivered a standard treatment regimen based solely on the patient's membership in a larger group. Selecting, in reference to a method of treatment as used herein, does not refer to fortuitous treatment of a patient having a particular criterion, but rather refers to the deliberate choice to administer treatment to a patient based on the patient having a particular criterion. Thus, selective treatment/administration differs from standard treatment/administration, which delivers a particular drug to all patients having a particular disease, regardless of their personal history, manifestations of disease, and/or biology.

Acne vulgaris is a chronic skin disease involving blockage and/or inflammation of pilosebaceous units (hair follicles and their accompanying sebaceous gland). It can present as noninflammatory lesions, inflammatory lesions, or a mixture of both, affecting mostly the face but also the back and chest. As used herein, the phrase "moderate to severe acne" means acne vulgaris with an Investigator's Global assessment (IGA) score of at least moderate (3) acne severity. As herein defined, "moderate to severe inflammatory acne" means acne vulgaris with inflammatory lesions (papules, pustules and nodules) and presence of non-inflammatory lesions (open and closed comedones) and an Investigator's Global assessment (IGA) score of at least moderate (3) acne severity " refers to inflammatory lesions (papules, pustules and nodules), and/or presence of non-inflammatory lesions (open and closed comedones). As used herein "acne" includes all forms of acne, e.g., P. *acnes, A. nodulocycstic, A. conglabata, A. fulminans*, pyoderma faciale, induced forms (e.g., chloracne or bromidacne and steroidacne, medication-induced acne rashes [e.g., observed with some cancer therapy]) and combinations of other diseases with acne, e.g., Synovitis-Acne-Pustulosis Hyperostosis-Osteitis (SAPHO), acne tetrad and follicular triad. As used herein "acne" also refers to non inflammatory and/or inflammatory acne.

IL-17 Antagonists

The various disclosed processes, kits, uses and methods utilize an IL-17 antagonist. IL-17 antagonists include small molecules and biological molecules that are capable of blocking, reducing and/or inhibiting IL-17 signal, activity and/or transduction. Examples of IL-17 antagonists include e.g., IL-17 binding molecules (e.g., soluble IL-17 receptors, IL-17 antibodies or antigen-binding fragments thereof, e.g., secukinumab or CJM112) and IL-17 receptor binding

molecules (e.g., IL-17 receptor antibodies or antigen-binding fragments thereof). In some embodiments, the IL-17 antagonist is an IL-17 binding molecule, preferably an IL-17 antibody or antigen-binding fragment thereof. IL-17 antibodies and antigen-binding fragment thereof as used herein can be fully-human, CDR-grafted, or chimeric. It is preferable that the constant region domains of an antibody or antigen-binding fragment thereof for use in the disclosed methods, uses, kits, etc. preferably comprise suitable human constant region domains, for instance as described in "Sequences of Proteins of Immunological Interest", Kabat E.A. et al, US Department of Health and Human Services, Public Health Service, National Institute of Health.

Particularly preferred IL-17 antibodies or antigen-binding fragments thereof used in the disclosed methods are human antibodies, especially secukinumab as described in Examples 1 and 2 of WO 2006/013107 and CJM112 as described in US Patent No 9,193,788, both of which are incorporated by reference herein in their entirety. Secukinumab and CJM112 are recombinant high-affinity, fully human monoclonal anti-human interleukin-17A (IL-17A, IL-17) antibodies of the IgG1/kappa isotype. Secukinumab has a high affinity for IL-17, i.e., a K_D of about 100-200 pM (e.g., about 200 pM), an IC_{50} of about 0.4 nM for *in vitro* neutralization of the biological activity of about 0.67 nM human IL-17A, and a half-life of about 4 weeks. CJM112 has a very high affinity for human IL-17A, i.e., about 1-10 pM (e.g., about 6 pM), and an *in vivo* half-life of about 2-4 weeks, e.g., about 3 weeks.

For ease of reference the amino acid sequences of the hypervariable regions of the secukinumab monoclonal antibody, based on the Kabat definition and as determined by the X-ray analysis and using the approach of Chothia and coworkers, as well as the V_L and V_H domains and full heavy and light chains, is provided in **Table 1**, below.

Light-Chain		
CDR1'	Kabat	R-A-S-Q-S-V-S-S-S-Y-L-A (SEQ ID NO:4)
	Chothia	R-A-S-Q-S-V-S-S-S-Y-L-A (SEQ ID NO:4)
CDR2'	Kabat	G-A-S-S-R-A-T (SEQ ID NO:5)

	Chothia	G-A-S-S-R-A-T (SEQ ID NO:5)
CDR2'	Kabat	Q-Q-Y-G-S-S-P-C-T (SEQ ID NO:6)
	Chothia	Q-Q-Y-G-S-S-P-C-T (SEQ ID NO:6)
Light Chain		Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro Cys Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg.
Heavy-Chain		
CDR1	Kabat	N-Y-W-M-N (SEQ ID NO:1)
CDR1-x	Chothia	G-F-T-F-S-N-Y-W-M-N (SEQ ID NO:11)
CDR2	Kabat	A-I-N-Q-D-G-S-E-K-Y-Y-V-G-S-V-K-G (SEQ ID NO:2)
CDR2-x	Chothia	A-I-N-Q-D-G-S-E-K-Y-Y (SEQ ID NO:12)
CDR3	Kabat	D-Y-Y-D-I-L-T-D-Y-Y-I-H-Y-W-Y-F-D-L (SEQ ID NO:3)
CDR3-x	Chothia	C-V-R-D-Y-Y-D-I-L-T-D-Y-Y-I-H-Y-W-Y-F-D-L-W-G (SEQ ID NO:13)
Heavy		Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro

chain		Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ala Ile Asn Gln Asp Gly Ser Glu Lys Tyr Tyr Val Gly Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg Asp Tyr Tyr Asp Ile Leu Thr Asp Tyr Tyr Ile His Tyr Trp Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser

Table 1: Amino acid sequences of the hypervariable regions of secukinumab. The DNA encoding the V_L of secukinumab is set forth in SEQ ID NO:9. The DNA encoding the V_H of secukinumab is set forth in SEQ ID NO:7.

In one embodiment, the IL-17 antibody or antigen-binding fragment thereof comprises at least one immunoglobulin heavy chain variable domain (V_H) comprising hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:1, said CDR2 having the amino acid sequence SEQ ID NO:2, and said CDR3 having the amino acid sequence SEQ ID NO:3. In one embodiment, the IL-17 antibody or antigen-binding fragment thereof comprises at least one immunoglobulin light chain variable domain ($V_{L'}$) comprising hypervariable regions CDR1', CDR2' and CDR3', said CDR1' having the amino acid sequence SEQ ID NO:4, said CDR2' having the amino acid sequence SEQ ID NO:5 and said CDR3' having the amino acid sequence SEQ ID NO:6. In one embodiment, the IL-17 antibody or antigen-binding fragment thereof comprises at least one immunoglobulin heavy chain variable domain (V_H) comprising hypervariable regions CDR1-x, CDR2-x and CDR3-x, said CDR1-x having the amino acid sequence SEQ ID NO:11, said CDR2-x having the amino acid sequence SEQ ID NO:12, and said CDR3-x having the amino acid sequence SEQ ID NO:13.

In one embodiment, the IL-17 antibody or antigen-binding fragment thereof comprises at least one immunoglobulin V_H domain and at least one immunoglobulin V_L domain, wherein: a) the immunoglobulin V_H domain comprises (e.g., in sequence): i) hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:1, said CDR2 having the amino acid sequence SEQ ID NO:2, and said CDR3 having the amino acid sequence SEQ ID NO:3; or ii) hypervariable regions CDR1-x, CDR2-x and CDR3-x, said CDR1-x having the

amino acid sequence SEQ ID NO:11, said CDR2-x having the amino acid sequence SEQ ID NO:12, and said CDR3-x having the amino acid sequence SEQ ID NO:13; and b) the immunoglobulin V_L domain comprises (e.g., in sequence) hypervariable regions CDR1', CDR2' and CDR3', said CDR1' having the amino acid sequence SEQ ID NO:4, said CDR2' having the amino acid sequence SEQ ID NO:5, and said CDR3' having the amino acid sequence SEQ ID NO:6.

In one embodiment, the IL-17 antibody or antigen-binding fragment thereof comprises: a) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:8; b) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:10; c) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:8 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:10; d) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3; e) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6; f) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13; g) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6; or h) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6.

In some embodiments, the IL-17 antibody or antigen-binding fragment thereof (e.g., secukinumab) comprises the three CDRs of SEQ ID NO:10. In other embodiments, the IL-17 antibody or antigen-binding fragment thereof comprises the three CDRs of SEQ ID NO:8. In other embodiments, the IL-17 antibody or antigen-binding fragment thereof comprises the three CDRs of SEQ ID NO:10 and the three CDRs of SEQ ID NO:8. CDRs of SEQ ID NO:8 and SEQ ID NO:10 may be found in **Table 1**. The free cysteine in the light chain (CysL97) may be seen in SEQ ID NO:6.

In some embodiments, IL-17 antibody or antigen-binding fragment thereof comprises the

light chain of SEQ ID NO:14. In other embodiments, the IL-17 antibody or antigen-binding fragment thereof comprises the heavy chain of SEQ ID NO:15. In other embodiments, the IL-17 antibody or antigen-binding fragment thereof comprises the light chain of SEQ ID NO:14 and the heavy domain of SEQ ID NO:15. In some embodiments, the IL-17 antibody or antigen-binding fragment thereof comprises the three CDRs of SEQ ID NO:14. In other embodiments, IL-17 antibody or antigen-binding fragment thereof comprises the three CDRs of SEQ ID NO:15. In other embodiments, the IL-17 antibody or antigen-binding fragment thereof comprises the three CDRs of SEQ ID NO:14 and the three CDRs of SEQ ID NO:15. CDRs of SEQ ID NO:14 and SEQ ID NO:15 may be found in **Table 1**.

Hypervariable regions may be associated with any kind of framework regions, though preferably are of human origin. Suitable framework regions are described in Kabat E.A. et al, ibid. The preferred heavy chain framework is a human heavy chain framework, for instance that of the secukinumab antibody. It consists in sequence, e.g. of FR1 (amino acid 1 to 30 of SEQ ID NO:8), FR2 (amino acid 36 to 49 of SEQ ID NO:8), FR3 (amino acid 67 to 98 of SEQ ID NO:8) and FR4 (amino acid 117 to 127 of SEQ ID NO:8) regions. Taking into consideration the determined hypervariable regions of secukinumab by X-ray analysis, another preferred heavy chain framework consists in sequence of FR1-x (amino acid 1 to 25 of SEQ ID NO:8), FR2-x (amino acid 36 to 49 of SEQ ID NO:8), FR3-x (amino acid 61 to 95 of SEQ ID NO:8) and FR4 (amino acid 119 to 127 of SEQ ID NO:8) regions. In a similar manner, the light chain framework consists, in sequence, of FR1' (amino acid 1 to 23 of SEQ ID NO:10), FR2' (amino acid 36 to 50 of SEQ ID NO:10), FR3' (amino acid 58 to 89 of SEQ ID NO:10) and FR4' (amino acid 99 to 109 of SEQ ID NO:10) regions.

In one embodiment, the IL-17 antibody or antigen-binding fragment thereof (e.g., secukinumab) is selected from a human IL-17 antibody that comprises at least: a) an immunoglobulin heavy chain or fragment thereof which comprises a variable domain comprising, in sequence, the hypervariable regions CDR1, CDR2 and CDR3 and the constant part or fragment thereof of a human heavy chain; said CDR1 having the amino acid sequence SEQ ID NO:1, said CDR2 having the amino acid sequence SEQ ID NO:2, and said CDR3 having the amino acid sequence SEQ ID NO:3; and b) an immunoglobulin light chain or fragment thereof which comprises a variable domain comprising, in sequence, the hypervariable

regions CDR1', CDR2', and CDR3' and the constant part or fragment thereof of a human light chain, said CDR1' having the amino acid sequence SEQ ID NO:4, said CDR2' having the amino acid sequence SEQ ID NO:5, and said CDR3' having the amino acid sequence SEQ ID NO:6.

In one embodiment, the IL-17 antibody or antigen-binding fragment thereof is selected from a single chain antibody or antigen-binding fragment thereof that comprises an antigen-binding site comprising: a) a first domain comprising, in sequence, the hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:1, said CDR2 having the amino acid sequence SEQ ID NO:2, and said CDR3 having the amino acid sequence SEQ ID NO:3; and b) a second domain comprising, in sequence, the hypervariable regions CDR1', CDR2' and CDR3', said CDR1' having the amino acid sequence SEQ ID NO:4, said CDR2' having the amino acid sequence SEQ ID NO:5, and said CDR3' having the amino acid sequence SEQ ID NO:6; and c) a peptide linker which is bound either to the N-terminal extremity of the first domain and to the C-terminal extremity of the second domain or to the C-terminal extremity of the first domain and to the N-terminal extremity of the second domain.

Alternatively, an IL-17 antibody or antigen-binding fragment thereof as used in the disclosed methods may comprise a derivative of the IL-17 antibodies set forth herein by sequence (e.g., a pegylated version of secukinumab or CJM112). Alternatively, the V_H or V_L domain of an IL-17 antibody or antigen-binding fragment thereof used in the disclosed methods may have V_H or V_L domains that are substantially identical to the V_H or V_L domains set forth in SEQ ID NO:8 and 10. A human IL-17 antibody disclosed herein may comprise a heavy chain that is substantially identical to that set forth as SEQ ID NO:15 and/or a light chain that is substantially identical to that set forth as SEQ ID NO:14. A human IL-17 antibody disclosed herein may comprise a heavy chain that comprises SEQ ID NO:15 and a light chain that comprises SEQ ID NO:14. A human IL-17 antibody disclosed herein may comprise: a) one heavy chain, comprising a variable domain having an amino acid sequence substantially identical to that shown in SEQ ID NO:8 and the constant part of a human heavy chain; and b) one light chain, comprising a variable domain having an amino acid sequence substantially identical to that shown in SEQ ID NO:10 and the constant part of a human light chain.

Alternatively, an IL-17 antibody or antigen-binding fragment thereof used in the disclosed methods may be an amino acid sequence variant of the reference IL-17 antibodies set

forth herein, as long as it contains CysL97. The disclosure also includes IL-17 antibodies or antigen-binding fragments thereof (e.g., secukinumab) in which one or more of the amino acid residues of the V_H or V_L domain of secukinumab (but not CysL97), typically only a few (e.g., 1-10), are changed; for instance by mutation, e.g., site directed mutagenesis of the corresponding DNA sequences. In all such cases of derivative and variants, the IL-17 antibody or antigen-binding fragment thereof is capable of inhibiting the activity of about 1 nM (= 30 ng/ml) human IL-17 at a concentration of about 50 nM or less, about 20 nM or less, about 10 nM or less, about 5 nM or less, about 2 nM or less, or more preferably of about 1 nM or less of said molecule by 50%, said inhibitory activity being measured on IL-6 production induced by hu-IL-17 in human dermal fibroblasts as described in Example 1 of WO 2006/013107.

In some embodiments, the IL-17 antibodies or antigen-binding fragments thereof, e.g., secukinumab, bind to an epitope of mature human IL-17 comprising Leu74, Tyr85, His86, Met87, Asn88, Val124, Thr125, Pro126, Ile127, Val128, His129. In some embodiments, the IL-17 antibody, e.g., secukinumab, binds to an epitope of mature human IL-17 comprising Tyr43, Tyr44, Arg46, Ala79, Asp80. In some embodiments, the IL-17 antibody, e.g., secukinumab, binds to an epitope of an IL-17 homodimer having two mature human IL-17 chains, said epitope comprising Leu74, Tyr85, His86, Met87, Asn88, Val124, Thr125, Pro126, Ile127, Val128, His129 on one chain and Tyr43, Tyr44, Arg46, Ala79, Asp80 on the other chain. The residue numbering scheme used to define these epitopes is based on residue one being the first amino acid of the mature protein (i.e., IL-17A lacking the 23 amino acid N-terminal signal peptide and beginning with Glycine). The sequence for immature IL-17A is set forth in the Swiss-Prot entry Q16552. In some embodiments, the IL-17 antibody has a K_D of about 100-200 pM. In some embodiments, the IL-17 antibody has an IC_{50} of about 0.4 nM for *in vitro* neutralization of the biological activity of about 0.67 nM human IL-17A. In some embodiments, the absolute bioavailability of subcutaneously (SC) administered IL-17 antibody has a range of about 60 – about 80%, e.g., about 76%. In some embodiments, the IL-17 antibody, such as secukinumab, has an elimination half-life of about 3-5 weeks, e.g., about 4 weeks (e.g., about 23 to about 35 days, about 23 to about 30 days, e.g., about 30 days). In some embodiments, the IL-17 antibody (such as secukinumab) has a T_{max} of about 7-8 days.

For ease of reference, the amino acid sequences of the hypervariable regions of the

CJM112 monoclonal antibody, based on the Kabat definition and the Chothia definition, as well as the V_L and V_H domains and full heavy and light chains are provided in **Table 2**, below.

CJM112 Light-Chain		
CDR1	Kabat	RPSQGINWELA (SEQ ID NO:16)
	Chothia	SQGINWE (SEQ ID NO:17)
CDR2	Kabat	DASSLEQ (SEQ ID NO:18)
	Chothia	DAS (SEQ ID NO:19)
CDR3	Kabat	QQFNSYPLT (SEQ ID NO:20)
	Chothia	FNSYPL (SEQ ID NO:21)
VL		AIQLTQSPSSLSASVGDRVTITCRPSQGINWELAWYQQ KPGKAPKLLIYDASSLEQGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQFNSYPLTFGGGTKVEIK (SEQ ID NO:22)
Light Chain		AIQLTQSPSSLSASVGDRVTITCRPSQGINWELAWY QQKPGKAPKLLIYDASSLEQGVPSRFSGSGSGTDFT LTISSLQPEDFATYYCQQFNSYPLTFGGGTKVEIKR TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:23)
CJM112 Heavy-Chain		
CDR1	Kabat	SYWMS (SEQ ID NO:24)
	Chothia	GFTFSSY (SEQ ID NO:25)

CDR2	Kabat	NIKQDGSEKYYVDSVKG (SEQ ID NO:26)
	Chothia	KQDGSE (SEQ ID NO:27)
CDR3	Kabat	DRGSLYY (SEQ ID NO:28)
	Chothia	DRGSLYY (SEQ ID NO:29)
VH		EVQLVESGGDLVQPGGSLRLSCAASGFTFSSYWMSWV RQAPGKGLEWVANIKQDGSEKYYVDSVKGRFTISRDN AKNSLYLQMNSLRAEDTAVYYCARDRGSLYYWGQGT LVTVSS (SEQ ID NO:30)
Heavy Chain		EVQLVESGGDLVQPGGSLRLSCAASGFTFSSYWMSWV RQAPGKGLEWVANIKQDGSEKYYVDSVKGRFTISRDN AKNSLYLQMNSLRAEDTAVYYCARDRGSLYYWGQGT LVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTV PSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTC PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK AKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSD IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:31)

Table 2: Amino acid sequences of the hypervariable regions (CDRs), variable domains (V_H and V_L) and full chains of CJM112.

In one embodiment, the IL-17 antibody or antigen-binding fragment thereof comprises at least one immunoglobulin heavy chain variable domain (V_H) comprising hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:24, said

CDR2 having the amino acid sequence SEQ ID NO:26, and said CDR3 having the amino acid sequence SEQ ID NO:28. In one embodiment, the IL-17 antibody or antigen-binding fragment thereof comprises at least one immunoglobulin heavy chain variable domain (V_H) comprising hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:25, said CDR2 having the amino acid sequence SEQ ID NO:27, and said CDR3 having the amino acid sequence SEQ ID NO:29.

In one embodiment, the IL-17 antibody or antigen-binding fragment thereof comprises at least one immunoglobulin light chain variable domain ($V_{L'}$) comprising hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:16, said CDR2 having the amino acid sequence SEQ ID NO:18 and said CDR3 having the amino acid sequence SEQ ID NO:20. In one embodiment, the IL-17 antibody or antigen-binding fragment thereof comprises at least one immunoglobulin light chain variable domain ($V_{L'}$) comprising hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:17, said CDR2 having the amino acid sequence SEQ ID NO:19 and said CDR3 having the amino acid sequence SEQ ID NO:21.

In one embodiment, the IL-17 antibody or antigen-binding fragment thereof comprises at least one immunoglobulin V_H domain and at least one immunoglobulin V_L domain, wherein: a) the immunoglobulin V_H domain comprises (e.g., in sequence): i) hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:24, said CDR2 having the amino acid sequence SEQ ID NO:26, and said CDR3 having the amino acid sequence SEQ ID NO:28; or ii) hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:25, said CDR2 having the amino acid sequence SEQ ID NO:27, and said CDR3 having the amino acid sequence SEQ ID NO:29; and b) the immunoglobulin V_L domain comprises (e.g., in sequence): i) hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:16, said CDR2 having the amino acid sequence SEQ ID NO:18, and said CDR3 having the amino acid sequence SEQ ID NO:20 or ii) hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:17, said CDR2 having the amino acid sequence SEQ ID NO:19, and said CDR3 having the amino acid sequence SEQ ID NO:21.

In one embodiment, the IL-17 antibody or antigen-binding fragment thereof comprises: a) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:30; b) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:22; c) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:30 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:22; d) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28; e) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20; f) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27 and SEQ ID NO:29; g) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21; h) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20; i) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27, and SEQ ID NO:29 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21; j) a light chain comprising SEQ ID NO:23; k) a heavy chain comprising SEQ ID NO:31; or l) a light chain comprising SEQ ID NO:23 and a heavy chain comprising SEQ ID NO:31.

In some embodiments, the IL-17 antibody or antigen-binding fragment thereof (e.g., CJM112) comprises the three CDRs of SEQ ID NO:22. In other embodiments, the IL-17 antibody or antigen-binding fragment thereof comprises the three CDRs of SEQ ID NO:30. In other embodiments, the IL-17 antibody or antigen-binding fragment thereof comprises the three CDRs of SEQ ID NO:22 and the three CDRs of SEQ ID NO:30. In some embodiments, the IL-17 antibody or antigen-binding fragment thereof comprises the three CDRs of SEQ ID NO:23. In other embodiments, IL-17 antibody or antigen-binding fragment thereof comprises the three CDRs of SEQ ID NO:31. In other embodiments, the IL-17 antibody or antigen-binding fragment thereof comprises the three CDRs of SEQ ID NO:23 and the three CDRs of SEQ ID NO:31.

In one embodiment, the IL-17 antibody or antigen-binding fragment thereof (e.g.,

CJM112) is selected from a human IL-17 antibody that comprises at least: a) an immunoglobulin heavy chain or fragment thereof which comprises a variable domain comprising, in sequence, the hypervariable regions CDR1, CDR2 and CDR3 and the constant part or fragment thereof of a human heavy chain; said CDR1 having the amino acid sequence SEQ ID NO:24, said CDR2 having the amino acid sequence SEQ ID NO:26, and said CDR3 having the amino acid sequence SEQ ID NO:28; and b) an immunoglobulin light chain or fragment thereof which comprises a variable domain comprising, in sequence, the hypervariable regions CDR1, CDR2, and CDR3 and the constant part or fragment thereof of a human light chain, said CDR1 having the amino acid sequence SEQ ID NO:16, said CDR2 having the amino acid sequence SEQ ID NO:18, and said CDR3 having the amino acid sequence SEQ ID NO:20.

In one embodiment, the IL-17 antibody or antigen-binding fragment thereof (e.g., CJM112) is selected from a human IL-17 antibody that comprises at least: a) an immunoglobulin heavy chain or fragment thereof which comprises a variable domain comprising, in sequence, the hypervariable regions CDR1, CDR2 and CDR3 and the constant part or fragment thereof of a human heavy chain; said CDR1 having the amino acid sequence SEQ ID NO:25, said CDR2 having the amino acid sequence SEQ ID NO:27 and said CDR3 having the amino acid sequence SEQ ID NO:29; and b) an immunoglobulin light chain or fragment thereof which comprises a variable domain comprising, in sequence, the hypervariable regions CDR1, CDR2, and CDR3 and the constant part or fragment thereof of a human light chain, said CDR1 having the amino acid sequence SEQ ID NO:17, said CDR2 having the amino acid sequence SEQ ID NO:19, and said CDR3 having the amino acid sequence SEQ ID NO:21.

In one embodiment, the IL-17 antibody or antigen-binding fragment thereof is selected from a single chain antibody or antigen-binding fragment thereof that comprises an antigen-binding site comprising: a) a first domain comprising, in sequence, the hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:24, said CDR2 having the amino acid sequence SEQ ID NO:26, and said CDR3 having the amino acid sequence SEQ ID NO:28; and b) a second domain comprising, in sequence, the hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:16, said CDR2 having the amino acid sequence SEQ ID NO:18, and said CDR3 having the amino acid sequence SEQ ID NO:20; and c) a peptide linker which is bound either to the N-terminal

extremity of the first domain and to the C-terminal extremity of the second domain or to the C-terminal extremity of the first domain and to the N-terminal extremity of the second domain.

In one embodiment, the IL-17 antibody or antigen-binding fragment thereof (e.g., CJM112) is selected from a single chain antibody or antigen-binding fragment thereof that comprises an antigen-binding site comprising: a) a first domain comprising, in sequence, the hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:25, said CDR2 having the amino acid sequence SEQ ID NO:27, and said CDR3 having the amino acid sequence SEQ ID NO:29; and b) a second domain comprising, in sequence, the hypervariable regions CDR1, CDR2 and CDR3, said CDR1 having the amino acid sequence SEQ ID NO:17, said CDR2 having the amino acid sequence SEQ ID NO:19, and said CDR3 having the amino acid sequence SEQ ID NO:21; and c) a peptide linker which is bound either to the N-terminal extremity of the first domain and to the C-terminal extremity of the second domain or to the C-terminal extremity of the first domain and to the N-terminal extremity of the second domain.

The V_H or V_L domain of an IL-17 antibody or antigen-binding fragment thereof used in the disclosed methods may have V_H and/or V_L domains that are substantially identical to the V_H or V_L domains set forth in SEQ ID NO:22 and 30. A human IL-17 antibody disclosed herein may comprise a heavy chain that is substantially identical to that set forth as SEQ ID NO:31 and/or a light chain that is substantially identical to that set forth as SEQ ID NO:23. A human IL-17 antibody disclosed herein may comprise a heavy chain that comprises SEQ ID NO:31 and a light chain that comprises SEQ ID NO:23. A human IL-17 antibody disclosed herein may comprise: a) one heavy chain, comprising a variable domain having an amino acid sequence substantially identical to that shown in SEQ ID NO:30 and the constant part of a human heavy chain; and b) one light chain, comprising a variable domain having an amino acid sequence substantially identical to that shown in SEQ ID NO:22 and the constant part of a human light chain.

In some embodiments of the disclosed uses, methods and kits, the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of IL-17 between residues Arg 55 and Trp 67, e.g., an epitope comprising Arg 55, Glu 57, and Trp 67. In some embodiments of the disclosed uses, methods and kits, the IL-17 antibody or antigen-binding fragment thereof binds

to an epitope comprising: Arg 55, Glu 57, Trp 67, Tyr 62, and Arg 101; Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, and Val 65; Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, Val 65, Val 22*, Leu 26, Asp 58, Glu 60, Pro 63, Pro 107, Phe 110, and Lys 114*, where amino acids marked with (*) designate residue contributed by the second IL-17 subunit of the homodimer IL-17A. The residue numbering scheme used to define these epitopes is based on residue one being the first amino acid of the mature protein (i.e., IL-17A lacking the 23 amino acid N-terminal signal peptide and beginning with Glycine). The sequence for immature IL-17A is set forth in the Swiss-Prot entry Q16552.

In some embodiments, the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 1-10 pM (e.g., about 6 pM). In some embodiments, the IL-17 antibody or antigen-binding fragment thereof has an *in vivo* half-life of about 2-4 weeks, e.g., about 3 weeks.

Other preferred IL-17 antagonists (e.g., antibodies) for use in the disclosed methods, kits and regimens are those set forth in US Patent Nos: 8,057,794; 7,767,206; 8,003,099; 8,110,191; and 7,838,638 and US Published Patent Application Nos: 20120034656 and 20110027290, which are incorporated by reference herein in their entirety.

Methods of Treatment and Uses of IL-17 Antagonists for Acne

The disclosed IL-17 antagonists, e.g., IL-17 binding molecules (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecules (e.g., IL-17 receptor antibody or antigen-binding fragment thereof), may be used *in vitro, ex vivo*, or incorporated into pharmaceutical compositions and administered *in vivo* to treat acne, e.g., moderate to severe inflammatory acne (e.g., human patients having acne).

The IL-17 antagonists, e.g., IL-17 binding molecules (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecules (e.g., IL-17 antibody or antigen-binding fragment thereof), may be used as a pharmaceutical composition when combined with a pharmaceutically acceptable carrier. Such a composition may contain, in addition to an IL-17 antagonist, carriers, various diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The characteristics of the carrier will depend on the route of administration. The pharmaceutical compositions for use in

the disclosed methods may also contain additional therapeutic agents for treatment of the particular targeted disorder. For example, a pharmaceutical composition may also include anti-inflammatory agents. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with the IL-17 binding molecules, or to minimize side effects caused by the IL-17 antagonists, e.g., IL-17 binding molecules (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecules (e.g., IL-17 antibody or antigen-binding fragment thereof).

Pharmaceutical compositions for use in the disclosed methods may be manufactured in conventional manner. In one embodiment, the pharmaceutical composition is provided in lyophilized form. For immediate administration it is dissolved in a suitable aqueous carrier, for example sterile water for injection or sterile buffered physiological saline. If it is considered desirable to make up a solution of larger volume for administration by infusion rather than a bolus injection, may be advantageous to incorporate human serum albumin or the patient's own heparinised blood into the saline at the time of formulation. The presence of an excess of such physiologically inert protein prevents loss of antibody by adsorption onto the walls of the container and tubing used with the infusion solution. If albumin is used, a suitable concentration is from 0.5 to 4.5% by weight of the saline solution. Other formulations comprise liquid or lyophilized formulation.

Antibodies, e.g., antibodies to IL-17, are typically formulated either in aqueous form ready for parenteral administration or as lyophilisates for reconstitution with a suitable diluent prior to administration. In some embodiments of the disclosed methods and uses, the IL-17 antagonist, e.g., IL-17 antibody, e.g., secukinumab or CJM112, is formulated as a lyophilisate. Suitable lyophilisate formulations can be reconstituted in a small liquid volume (e.g., 2 ml or less) to allow subcutaneous administration and can provide solutions with low levels of antibody aggregation. The use of antibodies as the active ingredient of pharmaceuticals is now widespread, including the products HERCEPTIN™ (trastuzumab), RITUXAN™ (rituximab), SYNAGIS™ (palivizumab), etc. Techniques for purification of antibodies to a pharmaceutical grade are well known in the art. When a therapeutically effective amount of an IL-17 antagonist, e.g., IL-17 binding molecules (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecules (e.g., IL-17 antibody or antigen-

binding fragment thereof) is administered by intravenous, cutaneous or subcutaneous injection, the IL-17 antagonist will be in the form of a pyrogen-free, parenterally acceptable solution. A pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection may contain, in addition to the IL-17 antagonist, an isotonic vehicle such as sodium chloride, Ringer's solution, dextrose, dextrose and sodium chloride, lactated Ringer's solution, or other vehicle as known in the art.

The appropriate dosage will vary depending upon, for example, the particular IL-17 antagonists, e.g., IL-17 binding molecules (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecules (e.g., IL-17 antibody or antigen-binding fragment thereof) to be employed, the host, the mode of administration and the nature and severity of the condition being treated, and on the nature of prior treatments that the patient has undergone. Ultimately, the attending health care provider will decide the amount of the IL-17 antagonist with which to treat each individual patient. In some embodiments, the attending health care provider may administer low doses of the IL-17 antagonist and observe the patient's response. In other embodiments, the initial dose(s) of IL-17 antagonist administered to a patient are high, and then are titrated downward until signs of relapse occur. Larger doses of the IL-17 antagonist may be administered until the optimal therapeutic effect is obtained for the patient, and the dosage is not generally increased further.

In practicing some of the methods of treatment or uses of the present disclosure, a therapeutically effective amount of an IL-17 antagonist, e.g., IL-17 binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof) is administered to a patient, e.g., a mammal (e.g., a human). While it is understood that the disclosed methods provide for treatment of acne patients using an IL-17 antagonist (e.g., secukinumab or CJM112), this does not preclude that, if the patient is to be ultimately treated with an IL-17 antagonist, such IL-17 antagonist therapy is necessarily a monotherapy. Indeed, if a patient is selected for treatment with an IL-17 antagonist, then the IL-17 antagonist (e.g., secukinumab or CJM112) may be administered in accordance with the methods of the disclosure either alone or in combination with other agents and therapies for treating acne patients, e.g., in combination with at least one additional acne agent or acne treatment, such as a topical acne agent, e.g., medicated

(anti-acne) creams, medicated cleansers or medicated soaps; an oral/systemic acne agent, e.g., antibiotics (such as doxycycline, tetracycline, lymecycline, minocycline, sarecycline or erythromycin), dapsone, oral zinc, oral retinoids (in particular isotretinoin); a systemic or lesional injected anti acne agent; systemic hormonal treatments, e.g., combined estrogen products and anti-androgens, such as spironolactone, finasteride and cyproterone acetate; or surgical, physical (such as ThermaClear™), light (including blue or UV light, photodynamic therapy [PDT]) or laser therapy. Other useful acne agents for combination (e.g., concurrent or sequential) with an IL-17 antagonist, e.g., IL-17 binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof) include tretinoin, adapalene, MBI 226, Retin-A Micro 0.04% facial acne treatment, M22-IPL, benzoyl peroxide, clindamycin, salicylic acid, JNJ 10229570-AAA, CB-03-01, ASC-J9, ARK-E021, aminolevulinic acid, BAY39-6251, RA-18C3, BLI1100, aminolevulinic acid HCL, SB204, tazarotene, lemuteporfin, CD0271, CD1579, S6G5T-3, -5, -7, FXFM244, azelaic acid (skinoren), YAZ (DRSP 3 mg/EE 0.02 mg, BAY86-5300), DRM01B, oxytetracycline, CD5789, CD0271, GK530G, drospirenone and ethinyl estradiol, sarecycline, P005672, CD5789, NVN1000, CTX-4430, norgestimate-ethinyl estradiol, cyproterone acetate-ethinyl estradiol, GI148512, BPX-01, apremilast, XPF-005, GSK2585823, PF-05175157, omiganan (CLS001) topical gel, tea tree oil, ANT-1207, GSK1940029, levamisole, cetuximab, PRK 124, MTC896, BLI1100-1, -2, -3; LEO43204, IDP-120, IDP-121, IDP-123, CLS001, B244, talarozole, radiation: VIS and wIRA, clotrimazole, gentamicin, beclomethasone, UVB irradiation, methyl aminolevulinate (MAL) PDT, GSK1940029, FMX101, ustekinumab, and combinations thereof.

When co-administered with one or more additional acne agents, an IL-17 antagonist may be administered either simultaneously with the other agent, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering the IL-17 antagonist in combination with other agents and the appropriate dosages for co-delivery. An IL-17 antagonist, e.g., IL-17 binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecule (e.g., IL-17 receptor antibody or antigen-binding fragment thereof) is conveniently administered parenterally, e.g., intravenously (e.g., into the antecubital or other peripheral vein),

intramuscularly, or subcutaneously. The duration of intravenous (IV) therapy using a pharmaceutical composition of the present disclosure will vary, depending on the severity of the disease being treated and the condition and personal response of each individual patient. Also contemplated is subcutaneous (SC) therapy using a pharmaceutical composition of the present disclosure. The health care provider will decide on the appropriate duration of IV or SC therapy and the timing of administration of the therapy, using the pharmaceutical composition of the present disclosure.

Preferred dosing and treatment regimens (including both induction and maintenance regimens) for treating acne patients using secukinumab are provided in PCT Application No. PCT/US2011/064307, which is incorporated by reference herein in its entirety.

The IL-17 antagonist, e.g., IL-17 binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecule (e.g., IL-17 receptor antibody or antigen-binding fragment thereof) may be administered to the acne patient as part of a loading regimen (an initial regimen designed to deliver drug quickly to target tissue – typically using more frequent dosing than employed for maintenance, but also sometimes using higher doses than employed for maintenance). For example, a loading regimen may employ unit subcutaneous (SC) dosing of about 75 mg to about 600 mg (e.g., about 75 mg, about 150 mg, about 300 mg, about 350 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg) of the IL-17 antibody (e.g., CJM112, Secukinumab (or a functional derivatives or biosimilar thereof, e.g. secukinumab or CJM112)).

In another example, the loading regimen employs unit intraveneous (IV) dosing of about 10mg/kg of the IL-17 antibody (e.g., CJM112, Secukinumab (or a functional derivatives or biosimilar thereof, e.g. secukinumab or CJM112))

The loading dose may be administered weekly or biweekly (every two weeks), e.g weekly. The loading dose may be administered during 1 to 8 weeks, e.g during 1 to 4 weeks, e.g 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, or 8 weeks. E.g the loading dose is administered weekly at weeks 0, 1, 2, 3, and 4.

In one specific embodiment, the IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112 (or a functional derivatives or biosimilar thereof, e.g. secukinumab or

CJM112), is administered subcutaneously, at an unit dose of about 75 mg to about 600 mg, during 2 to 8 weeks, e.g. during 4 to 8 weeks, e.g. during 4 or 5 weeks, e.g. at weeks 0, 1, 2, 3, and 4. Such an unit dose is for example administered weekly. The unit dose may also be administered every two weeks, or twice a week, or monthly.

In another embodiment, the IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112 (or a functional derivatives or biosimilar thereof, e.g. secukinumab or CJM112), is administered subcutaneously at an unit dose of about 150 mg to about 600 mg, during 2 to 8 weeks, e.g. during 4 to 8 weeks, e.g. during 4 or 5 weeks, e.g. at weeks 0, 1, 2, 3, and 4. Such an unit dose is for example administered weekly. The unit dose may also be administered every two weeks, or twice a week, or monthly.

In one specific embodiment, the IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112 (or a functional derivatives or biosimilar thereof, e.g. secukinumab or CJM112), is administered subcutaneously at an unit dose of about 300 mg to about 600 mg, during 2 to 8 weeks, e.g. during 4 to 8 weeks, e.g. during 4 or 5 weeks, e.g. at weeks 0, 1, 2, 3, and 4. Such an unit dose is for example administered weekly. The unit dose may also be administered every two weeks, or twice a week.

In another embodiment, the IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112 (or a functional derivatives or biosimilar thereof, e.g. secukinumab or CJM112), is administered subcutaneously at an unit dose of about 450 mg to about 600 mg, during 2 to 8 weeks, e.g. during 4 to 8 weeks, e.g. during 4 or 5 weeks, e.g. at weeks 0, 1, 2, 3, and 4. Such a dose is preferably administered weekly. The dose may also be administered every two weeks, or twice a week.

In another embodiment, the IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112 (or a functional derivatives or biosimilar thereof, e.g. secukinumab or CJM112), is administered subcutaneously at dose of about 300 mg to about 450 mg, during 2 to 8 weeks, e.g. during 4 to 8 weeks, e.g. during 4 or 5 weeks, e.g. at weeks 0, 1, 2, 3, and 4. Such a dose is preferably administered weekly. The dose may also be administered every two weeks, or twice a week.

Thereafter, a maintenance regimen is employed, and the patient is administered the IL-17 antibody, e.g. secukinumab or CJM112 (or a functional derivatives or biosimilar thereof, e.g. secukinumab or CJM112), subcutaneously at dose of about, subcutaneously at about 75 mg – about 600 mg (e.g., about 75 mg, about 150 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg). The maintenance regimen may be administered monthy, e.g. a dose of 75 mg – about 600 mg (e.g., about 75 mg, about 150 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg) is administered monthly.

As a result, the patient may be dosed subcutaneously with about 75 mg – about 600 mg (e.g., about 75 mg, about 150 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg) of the IL-17 antagonist (e.g., secukinumab or CJM112 (or a functional derivatives or biosimilar thereof, e.g. secukinumab or CJM112)) during weeks 0, 1, 2, 3, 4, 8, 12, 16, 20, etc.

Maintenance dosing may be less frequent than monthly, e.g., every other month, quarterly, bi-yearly, etc., which typically accompanies a higher of drug, e.g., 450 mg, 600 mg, etc.

Alternatively, the IL-17 antagonist, e.g., IL-17 binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecule (e.g., IL-17 receptor antibody or antigen-binding fragment thereof) may be administered to the acne patient without a loading regimen, e.g., the antagonist may be administered to the patient SC at about 75 mg to about 600 mg (e.g., about 75 mg, about 150 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg), e.g. every 4 weeks (monthly). In this manner, the patient is dosed SC with about 75 mg to about 600 mg (e.g., about 75 mg, about 150 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg) of the IL-17 antagonist (e.g., secukinumab or CJM112) during weeks 0, 4, 8, 12, 16, 20, etc.

Dosing may be less frequent than monthly, e.g., every other month, quarterly, bi-yearly, etc., which typically (but not necessarily) accompanies a higher of drug, e.g., 450 mg, 600 mg, etc.

In a preferred embodiment, the IL-17 antagonist is CJM112, which is administered without a loading regimen; preferably CJM112 is administered to the patient SC at about 75 mg to about 600 mg (e.g., about 75 mg, about 150 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg) every 4 weeks (monthly).

A typical duration of treatment is about of 6 months or less, e.g. about 12 to about 24 weeks, although both shoreter and longer courses of treatment may be employed, depending on a patient's response to therapy.

Alternatively, the IL-17 antagonist, e.g., IL-17 binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112 (or a functional derivatives or biosimilar thereof, e.g. secukinumab or CJM112)) or IL-17 receptor binding molecule (e.g., IL-17 receptor antibody or antigen-binding fragment thereof) may be administered to the acne patient as a single dose. For example the antagonist may be administered to the patient SC at a single dose of about 150 mg to about 600 mg (e.g., about 150 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg) once. In this manner, the patient is dosed SC with about 150 mg to about 600 mg (e.g., about 150 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg) of the IL-17 antagonist (e.g., secukinumab or CJM112) only one time. In another embodiment, the patient is dosed IV with about 10mg/kg. The patient would then be dosed again only when acne symptoms recur.

As herein defined, "unit dose" refers to a SC dose that can be comprised between about 75mg to 600 mg, e.g. about 150mg to about 600mg, e.g. about 150 mg to about 450 mg, e.g. about 300 mg to about 450 mg, or a e.g. about 75 mg to about 300 mg. For example an unit SC dose is about 75 mg, about 150 mg, about 300 mg, about 350 mg, about 400 mg, about 450mg, about 500 mg, about 550 mg, about 600 mg.

It will be understood that dose escalation may be appropriate for certain acne patients, e.g., patients that display inadequate response to treatment with the IL-17 antagonists, e.g., IL-17

binding molecules (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab and CJM112) or IL-17 receptor binding molecules (e.g., IL-17 receptor antibody or antigen-binding fragment thereof). Thus, SC dosages may be greater than about 75 mg to about 300 mg SC, e.g., about 80 mg, about 100 mg, about 125 mg, about 175 mg, about 200 mg, about 250 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 600 mg, etc.; similarly, IV (intraveneous) dosages may be greater than about 10 mg/kg, e.g., about 11 mg/kg, 12 mg/kg, 15 mg/kg, 20 mg/kg, 25 mg/kg, 30 mg/kg, 35 mg/kg, etc. It will also be understood that dose reduction may also be appropriate for certain acne patients, e.g., patients that display adverse events or an adverse response to treatment with the IL-17 antagonist (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112). Thus, dosages of the IL-17 antagonist (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112), may be less than about 75 mg to about 300 mg SC, e.g., about 25 mg, about 50 mg, about 80 mg, about 100 mg, about 125 mg, about 175 mg, about 200 mg, 250 mg, etc.

In some embodiments, the IL-17 antagonist, e.g., IL-17 binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecule (e.g., IL-17 receptor antibody or antigen-binding fragment thereof) may be administered to the patient at an initial dose of 75 mg delivered SC, and the dose may be then escalated to 150 mg or 300 mg if needed, as determined by a physician.

In some embodiments, the IL-17 antagonist, e.g., IL-17 binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecule (e.g., IL-17 receptor antibody or antigen-binding fragment thereof) may be administered to the patient at an initial dose of 150 mg delivered SC, and the dose may be then escalated to 450 mg or 600 mg if needed, as determined by a physician.

In some other embodiments, the IL-17 antagonist, e.g., IL-17 binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) or IL-17 receptor binding molecule (e.g., IL-17 receptor antibody or antigen-binding fragment thereof) may be administered to the patient at an initial dose of 300 mg delivered SC, and the dose may be then escalated to 450 mg or 600 mg if needed, as determined by a physician.

The timing of dosing is generally measured from the day of the first dose of secukinumab

or CJM112 (which is also known as "baseline"). However, health care providers often use different naming conventions to identify dosing schedules, as shown in **Table 3**.

Week	**0**/1	**1**/2	**2**/3	**3**/4	**4**/5	**5**/6	**6**/7	7/8	**8**/9	**9**/10	**10**/11	etc
1st day of week	0/**1**	7/**8**	14/**15**	21/**22**	28/**29**	35/**36**	42/**43**	49/**50**	56/**57**	63/**64**	70/**71**	etc.

Table 3: Common naming conventions for dosing regimens. Bolded items refer to the naming convention used herein.

Notably, week zero may be referred to as week one by some health care providers, while day zero may be referred to as day one by some health care providers. Thus, it is possible that different physicians will designate, e.g., a dose as being given during week 3 / on day 21, during week 3 / on day 22, during week 4 / on day 21, during week 4 / on day 22, while referring to the same dosing schedule. For consistency, the first week of dosing will be referred to herein as week 0, while the first day of dosing will be referred to as day 1. However, it will be understood by a skilled artisan that this naming convention is simply used for consistency and should not be construed as limiting, i.e., weekly dosing is the provision of a weekly dose of the IL-17 antibody regardless of whether the physician refers to a particular week as "week 1" or "week 2".

It will be understood that regimen changes may be appropriate for certain acne patients, e.g., patients that display inadequate response to treatment with the IL-17 antagonists, e.g., IL-17 binding molecules (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab and CJM112) or IL-17 receptor binding molecules (e.g., IL-17 receptor antibody or antigen-binding fragment thereof). Thus, administration (e.g for secukinumab or CJM112) may be more frequent than monthly dosing, e.g., bimonthly dosing (every two weeks) or weekly dosing.

Some patients may benefit from a loading regimen (e.g., weekly for several weeks [e.g., 1 to 5 weeks, e.g., dosing at weeks 0, 1, 2, 3 and/or 4] or biweekly for several weeks (e.g., 2 to 8 weeks, e.g., dosing at weeks 0, 2, 4, and/or 6) followed by maintenance regimen, e.g. a monthly maintenance regimen.

For example, an apropriate regimen for secukinumab or CJM112 can be weekly for several weeks [e.g., 1 to 5 weeks, e.g., dosing at weeks 0, 1, 2, 3 and/or 4] followed by a monthly maintenance regimen.

In another example, an apropriate regimen for secukinumab or CJM112 is biweekly for several weeks (e.g., 2 to 8 weeks, e.g., dosing at weeks 0, 2, 4, and/or 6) followed by a monthly maintenance regimen.

It will also be understood that administration (e.g for secukinumab or CJM112) may be less frequent than monthly dosing, e.g., dosing every 6 weeks, every 8 weeks (every two months), quarterly (every three months), etc.

Patients' responses to treatment may be assessed using patient reported outcomes. For example the Dermatology Life Quality Index (DLQI), Patient global assessment, Patient's satisfaction questionnaire,. Patient's responses to treatment may also be assessed by analyzing the acne severity in different areas of the body (Investigator Global Assessment (IGA) on the face [achievement of clear or almost clear; or 2 grade improvement from baseline] and Comprehensive Acne severity scale (CASS) on the trunk [Tan et al. (2007) J Cutan Med Surg. 11(6): 211-6]) and also the numbers of lesions (inflammatory [papules, pustules, nodules]) and their type in the different anatomical areas. A therapeutic effect in inflammatory acne exists when there is a reduction in inflammatory lesions (typically inflammatory facial lesions).

Disclosed herein are methods of treating and/or preventing acne, e.g. non-inflammatory acne, inflammatory acne or non-inflammatory and inflammatory acne, comprising administering an IL-17 antagonist to a patient in need thereof. In some embodiments, the IL-17 antagonist is an IL-17 antibody or antigen-binding fragment thereof, e.g. secukinumab or CJM112.

Additionally disclosed herein are methods of treating and/or preventing a patient having acne, e.g., moderate to severe inflammatory acne, e.g. non-inflammatory acne, inflammatory acne or non-inflammatory and inflammatory acne, comprising administering an IL-17 antibody or antigen-binding fragment thereof to a patient in need thereof, wherein the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of mature IL-17: a) between residues Arg 55 and Trp 67; b) comprising Arg 55, Glu 57, and Trp 67; c) comprising Arg 55, Glu 57, Trp 67,

Tyr 62, and Arg 101; d) comprising Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, and Val 65; or e) comprising Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, Val 65, Val 22*, Leu 26, Asp 58, Glu 60, Pro 63, Pro 107, Phe 110, and Lys 114*, where amino acids marked with (*) designate a residue contributed by the second IL-17 subunit of the IL-17A homodimer), wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 1-10 pM (e.g., about 6 pM) and an *in vivo* half-life of about 2-4 weeks, e.g., about 3 weeks.

Additionally disclosed herein are IL-17 antagonists (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., CJM112) for use in treating a patient having acne, e.g., moderate to severe inflammatory acne, wherein the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of mature IL-17: a) between residues Arg 55 and Trp 67; b) comprising Arg 55, Glu 57, and Trp 67; c) comprising Arg 55, Glu 57, Trp 67, Tyr 62, and Arg 101; d) comprising Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, and Val 65; or e) comprising Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, Val 65, Val 22*, Leu 26, Asp 58, Glu 60, Pro 63, Pro 107, Phe 110, and Lys 114*, where amino acids marked with (*) designate a residue contributed by the second IL-17 subunit of the IL-17A homodimer), wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 1-10 pM (e.g., about 6 pM) and an *in vivo* half-life of about 2-4 weeks, e.g., about 3 weeks.

Additionally disclosed herein are IL-17 antagonists (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., CJM112) for use in the manufacture of a medicament for treating a patient having acne, e.g., moderate to severe inflammatory acne, wherein the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of mature IL-17: a) between residues Arg 55 and Trp 67; b) comprising Arg 55, Glu 57, and Trp 67; c) comprising Arg 55, Glu 57, Trp 67, Tyr 62, and Arg 101; d) comprising Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, and Val 65; or e) comprising Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, Val 65, Val 22*, Leu 26, Asp 58, Glu 60, Pro 63, Pro 107, Phe 110, and Lys 114*, where amino acids marked with (*) designate a residue contributed by the second IL-17 subunit of the IL-17A homodimer), wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 1-10 pM (e.g., about 6 pM) and an *in vivo* half-life of about 2-4 weeks, e.g., about 3 weeks.

Additionally disclosed herein are IL-17 antagonists (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) for use in the manufacture of a medicament for treating and/or preventing a patient having acne, e.g., moderate to severe inflammatory acne, e.g. non-inflammatory acne, inflammatory acne or non-inflammatory and inflammatory acne, wherein the medicament is formulated to comprise containers, each container having a sufficient amount of the IL-17 antagonist (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) to allow subcutaneous delivery of at least about 75 mg – about 600 mg (e.g., about 75 mg, about 150 mg, about 300 mg, about 450 mg, about 600 mg), preferably about 75 mg – about 300 mg, of the IL-17 antagonist (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) per unit dose, and further wherein the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of mature IL-17: a) between residues Arg 55 and Trp 67; b) comprising Arg 55, Glu 57, and Trp 67; c) comprising Arg 55, Glu 57, Trp 67, Tyr 62, and Arg 101; d) comprising Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, and Val 65; or e) comprising Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, Val 65, Val 22*, Leu 26, Asp 58, Glu 60, Pro 63, Pro 107, Phe 110, and Lys 114*, where amino acids marked with (*) designate a residue contributed by the second IL-17 subunit of the IL-17A homodimer), wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 1-10 pM (e.g., about 6 pM) and an *in vivo* half-life of about 2-4 weeks, e.g., about 3 weeks.

Disclosed herein are methods of treating and/or preventing a patient having acne, e.g., moderate to severe inflammatory acne, comprising administering an IL-17 antibody or antigen-binding fragment thereof to a patient in need thereof, wherein the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of an IL-17 homodimer having two mature IL-17 protein chains, said epitope comprising Leu74, Tyr85, His86, Met87, Asn88, Val124, Thr125, Pro126, Ile127, Val128, His129 on one chain and Tyr43, Tyr44, Arg46, Ala79, Asp80 on the other chain, wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 100-200 pM, and wherein the IL-17 antibody or antigen-binding fragment thereof has an *in vivo* half-life of about 4 weeks.

Additionally disclosed herein are IL-17 antagonists (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) for use in treating and/or preventing a

patient having acne, e.g., moderate to severe acne, e.g. non-inflammatory acne, inflammatory acne or non-inflammatory and inflammatory acne, wherein the IL-17 antagonist (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) binds to an epitope of an IL-17 homodimer having two mature IL-17 protein chains, said epitope comprising Leu74, Tyr85, His86, Met87, Asn88, Val124, Thr125, Pro126, Ile127, Val128, His129 on one chain and Tyr43, Tyr44, Arg46, Ala79, Asp80 on the other chain, wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 100-200 pM, and wherein the IL-17 antibody or antigen-binding fragment thereof has an *in vivo* half-life of about 4 weeks.

Additionally disclosed herein are IL-17 antagonists (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) for use in the manufacture of a medicament for treating and/or preventing a patient having acne, e.g., moderate to severe acne, e.g. non-inflammatory acne, inflammatory acne or non-inflammatory and inflammatory acne, wherein the IL-17 antagonist (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) binds to an epitope of an IL-17 homodimer having two mature IL-17 protein chains, said epitope comprising Leu74, Tyr85, His86, Met87, Asn88, Val124, Thr125, Pro126, Ile127, Val128, His129 on one chain and Tyr43, Tyr44, Arg46, Ala79, Asp80 on the other chain, wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 100-200 pM, and wherein the IL-17 antibody or antigen-binding fragment thereof has an *in vivo* half-life of about 4 weeks.

Additionally disclosed herein are IL-17 antagonists (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) for use in the manufacture of a medicament for treating and/or preventing a patient having acne, e.g., moderate to severe acne, e.g. non-inflammatory acne, inflammatory acne or non-inflammatory and inflammatory acne, wherein the medicament is formulated to comprise containers, each container having a sufficient amount of the IL-17 antagonist (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) to allow subcutaneous delivery of at least about 75 mg – about 300 mg (e.g., about 75 mg, about 150 mg, about 300 mg, about 450 mg, about 600 mg), preferably about 75 mg – about 300 mg, of the IL-17 antagonist (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) per unit dose, and further wherein the IL-17 antagonist (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112) binds

to an epitope of an IL-17 homodimer having two mature IL-17 protein chains, said epitope comprising Leu74, Tyr85, His86, Met87, Asn88, Val124, Thr125, Pro126, Ile127, Val128, His129 on one chain and Tyr43, Tyr44, Arg46, Ala79, Asp80 on the other chain, wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 100-200 pM, and wherein the IL-17 antibody or antigen-binding fragment thereof has an *in vivo* half-life of about 4 weeks.

As used herein, the phrase "formulated at a dosage to allow [route of administration] delivery of [a designated dose]" is used to mean that a given pharmaceutical composition can be used to provide a desired dose of an IL-17 antagonist, e.g., an IL-17 antibody, e.g., secukinumab or CJM112, via a designated route of administration (e.g., SC or IV). As an example, if a desired subcutaneous dose is 300 mg, then a clinician may use 2 ml of an IL-17 antibody formulation having a concentration of 150 mg/ml, 1 ml of an IL-17 antibody formulation having a concentration of 300 mg/ml, 0.5 ml of an IL-17 antibody formulation having a concentration of 600 mg/ml, etc. In each such case, these IL-17 antibody formulations are at a concentration high enough to allow subcutaneous delivery of the IL-17 antibody. Subcutaneous delivery typically requires delivery of volumes of less than about 2 ml, preferably a volume of about 1 ml or less. Preferred formulations are liquid pharmaceutical compositions comprising: a) about 25 mg/mL to about 150 mg/mL secukinumab, about 10 mM to about 30 mM histidine pH 5.8, about 200 mM to about 225 mM trehalose, about 0.02% polysorbate 80, and about 2.5 mM to about 20 mM methionine; and b) about 150 mg/mL CJM112, 4.8 mM L-histidine, 15.2 mM L-histidine-HCl 220 mM sucrose and 0.04% polysorbate 20, at pH 6.0 ± 0.5.

As used herein, the phrase "container having a sufficient amount of the IL-17 antagonist to allow delivery of [a designated dose]" is used to mean that a given container (e.g., vial, pen, syringe) has disposed therein a volume of an IL-17 antagonist (e.g., as part of a pharmaceutical composition) that can be used to provide a desired dose. As an example, if a desired dose is 150 mg, then a clinician may use 2 ml from a container that contains an IL-17 antibody formulation with a concentration of 75 mg/ml, 1 ml from a container that contains an IL-17 antibody formulation with a concentration of 150 mg/ml, 0.5 ml from a container contains an IL-17 antibody formulation with a concentration of 300 mg/ml, etc. In each such case, these containers have a sufficient amount of the IL-17 antagonist to allow delivery of the desired 150 mg dose.

In some embodiments of the disclosed uses, methods, and kits, the patient has moderate to severe acne, e.g. moderate to severe inflammatory acne.

In some embodiments of the disclosed uses, methods, and kits, the patient was previously treated for acne with a topical anti-acne treatment, an oral/systemic anti-acne treatment, a systemic or lesional injected anti-acne treatment, or surgical, physical, light or laser therapy.

In some embodiments of the disclosed uses, methods, and kits, the patient is monthly administered about 75 mg – about 600 mg (e.g., about 75 mg, about 150 mg, about 300 mg, about 450 mg, about 600mg), preferably about 75 mg – about 300 mg, of the IL-17 antibody or antigen-binding fragment thereof (e.g., secukinumab or CJM112) by subcutaneous injection. For example, this regimen can be administered for a period of 1 to 24 weeks, e.g about 12 to about 24 weeks.

In some embodiments of the disclosed uses, methods, and kits, the patient is monthly administered about 75 mg (e.g., 75 mg) of the IL-17 antibody or antigen-binding fragment thereof (e.g., secukinumab or CJM112) by subcutaneous injection. For example, this regimen can be administered for a period of 1 to 24 weeks, e.g about 12 to about 24 weeks.

In some embodiments of the disclosed uses, methods, and kits, the patient is monthly administered about 150 mg (e.g., 150 mg) of the IL-17 antibody or antigen-binding fragment thereof (e.g., secukinumab or CJM112) by subcutaneous injection. For example, this regimen can be administered for a period of 1 to 24 weeks, e.g about 12 to about 24 weeks.

In some embodiments of the disclosed uses, methods, and kits, the patient is monthly administered about 300 mg (e.g., 300 mg) of the IL-17 antibody or antigen-binding fragment thereof (e.g., secukinumab or CJM112) by subcutaneous injection. For example, this regimen can be administered for a period of 1 to 24 weeks, e.g about 12 to about 24 weeks.

In some embodiments of the disclosed uses, methods, and kits, the patient is monthly administered about 400 mg (e.g., 400 mg) of the IL-17 antibody or antigen-binding fragment thereof (e.g., secukinumab or CJM112) by subcutaneous injection. For example, this regimen can be administered for a period of 1 to 24 weeks, e.g about 12 to about 24 weeks.

In some embodiments of the disclosed uses, methods, and kits, the patient is monthly administered about 450 mg (e.g., 450 mg) of the IL-17 antibody or antigen-binding fragment

thereof (e.g., secukinumab or CJM112) by subcutaneous injection. For example, this regimen can be administered for a period of 1 to 24 weeks, e.g about 12 to about 24 weeks.

In some embodiments of the disclosed uses, methods, and kits, the patient is monthly administered about 500 mg (e.g., 500 mg) of the IL-17 antibody or antigen-binding fragment thereof (e.g., secukinumab or CJM112) by subcutaneous injection. For example, this regimen can be administered for a period of 1 to 24 weeks, e.g about 12 to about 24 weeks.

In some embodiments of the disclosed uses, methods, and kits, the patient is monthly administered about 600 mg (e.g., 600 mg) of the IL-17 antibody or antigen-binding fragment thereof (e.g., secukinumab or CJM112) by subcutaneous injection. For example, this regimen can be administered for a period of 1 to 24 weeks, e.g about 12 to about 24 weeks.

In some embodiments of the disclosed uses, methods, and kits, the patient is monthly administered about 10mg/kg (e.g., 10mg/kg) of the IL-17 antibody or antigen-binding fragment thereof (e.g., secukinumab or CJM112) by intraveneous injection.

In some embodiments of the disclosed uses, methods, and kits, the patient is given a single administration of about 150 mg – about 600 mg (e.g., about 150 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg) of the IL-17 antibody or antigen-binding fragment thereof (e.g., secukinumab or CJM112) by subcutaneous injection.

In some embodiments of the disclosed uses, methods, and kits, the IL-17 antibody or antigen-binding fragment thereof comprises: i) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:30; ii) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:22; iii) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:30 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:22; iv) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28; v) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID

NO:20; vi) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27 and SEQ ID NO:29; vii) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21; viii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20; ix) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27, and SEQ ID NO:29 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21; x) a light chain comprising SEQ ID NO:23; xi) a heavy chain comprising SEQ ID NO:31; or xii) a light chain comprising SEQ ID NO:23 and a heavy chain comprising SEQ ID NO:31. In some embodiments of the disclosed uses, methods, and kits, the IL-17 antibody or antigen-binding fragment thereof is CJM112.

In some embodiments of the disclosed uses, methods, and kits, the IL-17 antibody or antigen-binding fragment thereof comprises: i) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:8; ii) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:10; iii) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:8 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:10; iv) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3; v) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6; vi) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13; vii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6; viii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6; ix) an immunoglobulin light chain comprising the amino acid

sequence set forth as SEQ ID NO:14; x) an immunoglobulin heavy chain comprising the amino acid sequence set forth as SEQ ID NO:15; or xi) an immunoglobulin light chain comprising the amino acid sequence set forth as SEQ ID NO:14 and an immunoglobulin heavy chain comprising the amino acid sequence set forth as SEQ ID NO:15. In some embodiments of the disclosed uses, methods, and kits, the IL-17 antibody or antigen-binding fragment thereof is secukinumab.

Disclosed herein are also methods of treating and/or preventing a patient having moderate to severe acne, e.g. non-inflammatory acne, inflammatory acne or non-inflammatory and inflammatory acne, e.g. moderate to severe inflammatory acne, comprising monthly administering to the patient about 150 mg to about 600 mg of CJM112 CJM112 (or a functional derivatives or biosimilar thereof) by subcutaneous injection.

Furtheremore are disclosed herein are methods of treating and/or preventing a patient having moderate to severe acne, e.g. non-inflammatory acne, inflammatory acne or non-inflammatory and inflammatory acne, e.g. moderate to severe inflammatory acne, comprising monthly administering to the patient about 10 mg/kg of CJM112 (or a functional derivatives or biosimilar thereof) by intraveneous injection.

Disclosed herein are also methods of treating and/or preventing a patient having moderate to severe acne, e.g. non-inflammatory acne, inflammatory acne or non-inflammatory and inflammatory acne, e.g. moderate to severe inflammatory acne, comprising monthly administering to the patient about 150 mg to about 600 mg of secukinumab (or a functional derivatives or biosimilar thereof) by subcutaneous injection.

Furtheremore are disclosed herein are methods of treating and/or preventing a patient having moderate to severe acne, e.g. non-inflammatory acne, inflammatory acne or non-inflammatory and inflammatory acne, e.g. moderate to severe inflammatory acne, comprising monthly administering to the patient about 10 mg/kg of Secukinumab (or a functional derivatives or biosimilar thereof§) by intraveneous injection.

Kits

The disclosure also encompasses kits for treating acne, e.g., moderate to severe acne, e.g. non-inflammatory acne, inflammatory acne or non-inflammatory and inflammatory acne, e.g. moderate to severe inflammatory acne. Such kits comprise an IL-17 antagonist, e.g., IL-17 binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112, or IL-17 receptor binding molecule (e.g., IL-17 antibody or antigen-binding fragment thereof) (e.g., in liquid or lyophilized form) or a pharmaceutical composition comprising the IL-17 antagonist (described *supra).* Additionally, such kits may comprise means for administering the IL-17 antagonist (e.g., an autoinjector, a syringe and vial, a prefilled syringe, a prefilled pen) and instructions for use. These kits may contain additional therapeutic agents (described *supra*) for treating acne, e.g., for delivery in combination with the enclosed IL-17 antagonist, e.g., IL-17 binding molecule, e.g., IL-17 antibody, e.g., secukinumab or CJM112. Such kits may also comprise instructions for administration of the IL-17 antagonist (e.g., IL-17 antibody, e.g., secukinumab or CJM112) to treat acne, e.g., moderate to severe inflammatory acne. Such instructions may provide the dose (e.g., 10 mg/kg, 75 mg, 150 mg, 300 mg, 450 mg, 600 mg), route of administration (e.g., IV, SC), and dosing regimen (e.g., monthly with or without an induction regimen) for use with the enclosed IL-17 antagonist, e.g., IL-17 binding molecule, e.g., IL-17 antibody, e.g., secukinumab or CJM112.

The phrase "means for administering" is used to indicate any available implement for systemically administering a drug to a patient, including, but not limited to, a pre-filled syringe, a vial and syringe, an injection pen, an autoinjector, an IV drip and bag, a pump, etc. With such items, a patient may self-administer the drug (i.e., administer the drug without the assistance of a physican) or a medical practitioner may administer the drug.

The phrase "therapeutically effective amount" is used to indicate a quantity of drug that can achieve a given stated effect, e.g., treatment of acne.

Disclosed herein are kits for use in treating and/or preventing a patient having acne, e.g., moderate to severe inflammatory acne, comprising an IL-17 antagonist (e.g., IL-17 binding molecule, e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112. In some embodiments, the kit further comprises means for administering the IL-17 antagonist to the patient. In some embodiments, the kit further comprises instructions for

administration of the IL-17 antagonist, wherein the instructions indicate that the IL-17 antagonist (e.g., IL-17 binding molecule, e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112, is to be administered to the patient SC with or without a loading regimen, e.g., at about 75 mg – about 600 mg (e.g., about 75 mg, about 150 mg, about 300 mg, about 450 mg, about 600 mg) every 4 weeks (monthly). In some embodiments, the kit further comprises instructions for administration of the IL-17 antagonist, wherein the instructions indicate that the IL-17 antagonist (e.g., IL-17 binding molecule, e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., secukinumab or CJM112, is to be administered a single time (once) to the patient SC with or without a loading regimen, e.g., at about 150 mg – about 600 mg (e.g., about 150 mg, about 300 mg, about 450 mg, about 600 mg). In some embodiments, the instructions will provide for dose escalation or dose reduction as needed, to be determined by a physician.

Methods of Treatment and Uses of IL-17 Antagonists for Further Indications

The disclosed IL-17 antagonists, e.g., IL-17 binding molecules (e.g., IL-17 antibody or antigen-binding fragment thereof, e.g., Secukinumab, CJM112, or a functional derivatives or biosimilar thereof, e.g. secukinumab or CJM112) or IL-17 receptor binding molecules (e.g., IL-17 receptor antibody or antigen-binding fragment thereof), may be used *in vitro*, *ex vivo*, or incorporated into pharmaceutical compositions and administered *in vivo* to treat cutaneous lupus erythematosus, skin sarcoidosis, vitiligo, atopic dermatitis, Pityriasis rubra pilaris, entheseal and tendon inflammation (e.g., enthesitis, tendenitis) and injury, keloids, non-melanoma skin cancer (NMSC), aphthous diseases, in particular chronic aphthous stomatitis, lichen planus with its variants, such as oral erosive lichen, alopecia areata, neutrophilic dermatoses, such as Sweet syndrome (acute febrile neutrophilic dermatosis); Pyoderma gangraenosum; Sneddon-Wilkinson syndrome, Behçet disease, different forms of inflammatory rosacea, including rosacea fulminans, or inflammatory papulopustular rosacea, Acute macular degeneration, Alzheimers Disease, Artherosclerosis, Cardiomypathies, Autism, Biliary Cirrhosis, Bronchiolytis Obliterans, Bullous Pemphigoid, Dental diseases (chronic periodontal disease, preidontitis, bone loss), Enthesitis, Tendenitis, Epilepsy, Fibrosis e.g. lung fibrosis, NASH (non-alcoholic steatohepatitis), Guillain-Barre-Syndrome, GVHD, JIA, SLE, Lupus, Lupus Nephritis, Netherton Syndrome, icthyothis,

Neuromyelitis Optica, Lichen Planus, Myastenia Gravis, Pyoderma Gangrenosum, Rosacea, Sarcoidosis, Sjoegren's Syndrome, Stroke, Transplantation, Type-1 Diabetes, Wound healing, esophagitis, including Barrett' esophagus and esophageal cancer, and cancers of the hypopharynx, Alpha-1-antitrypsin deficiency, Septic shock, Injuries and skin wounds, Enteritis of small intestine, Colitis, Inflammatory bowel disease, Appendicitis, Barrett's esophagus, Crohn's disease, Whipple's disease, Gastrointestinal hemorrhage, Polyp of intestine, Gastritis, Cholestasis, disorders of the of intestine, Ascites, Disease of mouth, Irritable bowel syndrome, Eruption, Wounds of skin, disorders of the of mucous membrane, Eczema, Contact dermatitis, Dermatitis, Autoimmune skin disease, Lamellar ichthyosis, Neurocutaneous syndrome, Genodermatosis, Brucellosis, Staphylococcal infectious disease, Infection due to Haemophilus, Infection due to Enterobacteriaceae, Disease due to Gram-positive bacteria, Chlamydial infection, Infection due to Pseudomonas, Bacterial infectious disease, Helicobacter pylori gastrointestinal tract infection, Streptococcal infectious disease, Tularemia, Disease caused by rickettsiae, Bacterial infection due to Bacillus, Salmonella infection, Mycobacteriosis, Listeriosis, Bacteremia, Disease due to Neisseria, Bordetellosis, Disease due to Gram-negative bacteria, Infection due to Bacteroides, Crohn's disease, Polymyositis, Rheumatoid arthritis, Lupus erythematosus, Wegener's granulomatosis, Diabetes mellitus type 1, Idiopathic thrombocytopenic purpura, Graves' disease, Autoimmune endocrine disease, Infectious disease of lung, Lower respiratory tract infection, Severe acute respiratory syndrome, Pneumonia, Interstitial lung disease, Injury of lung, Chronic sinusitis, Pulmonary embolism, Chronic obstructive pulmonary disease, Pulmonary hypertension, Hypoxia, Pulmonary thromboembolism, Ebola virus disease, Epstein-Barr virus infection, Viral disease, Influenza, Disease due to Rotavirus, Herpes simplex type 2 infection, Disease due to Orthopoxvirus, Disease due to Picornaviridae, Disease due to Paramyxoviridae, Disease due to Rhinovirus, Respiratory syncytial virus infection, Disease due to West Nile virus, Measles, Cytomegalovirus infection, Sendai virus infection, Disease due to Adenovirus, Herpes simplex, Rift valley fever, Viral infections of the central nervous system, viremia, human papilloma virus (HPV), Viral cardiovascular infection, Toxoplasmosis, Infection by Encephalitozoon cuniculi, Malaria, Disease due to Trypanosomatidae, Disease caused by parasite, Helminth infection, Infection by Nippostrongylus, Allergic disorder, Systemic inflammatory response syndrome, Inflammatory

disorder, Delayed hypersensitivity disorder, Multiple myeloma/plasmacytoma, Malignant tumor of intestine, cancer of the liver, gastric cancer, primary malignant neoplasm of bone, brain cancer, Bladder cancer, Thyroid cancer, Skin cancer, T-cell lymphoma, Malignant tumor of spleen, B-cell lymphoma, Pancreatic cancer, Kidney cancer, ovarian cancer, retinoblastoma, testicular cancer, Shock, disorders of cardiac function, Cardiomyopathy, Injury of heart, Ischemia, Myocardial ischemia, Arrhythmogenic right ventricular dysplasia, carditis, endocarditis, Heart disease, Atherosclerotic occlusive disease, Cardiomegaly, Hypertensive disorder, Aneurysm, Cardiovascular disease, arterial stricture, dilated cardiomyophathy, Coronary arteriosclerosis, Proteinuria syndrome, Urogenital injury, Chronic interstitial cystitis, Cystic disease of kidney, Nephrotic syndrome, Kidney transplant failure and rejection, Kidney disease, Renal tubular disorder, Undescended testicle, Nerve injury, Meningitis, Neuropathy, Hypoxia of brain, Cerebrovascular disease, disorders of the basal ganglia, Parkinson's disease, disorders of the of brain, Movement disorder, Prion disease, Huntington's disease, Multiple sclerosis, Alzheimer's disease, Encephalitis, Paralytic syndrome, Spinocerebellar ataxia, Encephalomyelopathy, Stachybotryotoxicosis, Aspergillosis, Candidiasis, Toxic effect of mycotoxin, Non-fatal electric shock, Effects of heat, Poisoning by drug AND/OR medicinal substance, Toxic nephropathy, Radiation injury, Effects of reduced temperature, Drug abuse, Drug resistance to insulin, Ischemic reperfusion injury, Deficiency of carboxylesterase, High fat diet, Deficiency of glutamate-ammonia ligase, Lysinuric protein intolerance, Hyperoxia, Hypervolemia, Hyperlipidemia, Hutchinson-Gilford syndrome, Diabetes mellitus type 1, Obesity, Ketogenic diet, Osteoporosis, Congenital glucose-galactose malabsorption, Iron overload, amuloidosis, Dehydration, Mucopolysaccharidosis, Goiter, Rickets, Otitis media, Injury of external ear, Perforation of tympanic membrane, Otosclerosis, Abscess, Multiple organ, failure, Endometriosis, disorders related to transplantation, Inflammatory disease of liver, Injury of liver, Liver regeneration, Hepatocellular dysplasia, Liver transplant disorder, Non-alcoholic fatty liver, disorders of iron metabolism, Steatosis of liver, Arthropathy, Osteomyelitis, Rheumatoid arthritis, Systemic lupus erythematosus, Osteopenia, Muscle atrophy, Myopathy, Injury of musculoskeletal system, bleeding, sarcoidosis, primary immune deficiency disorder thrombosis, anemia, Graft versus host disease, Lymphadenitis, Hemorrhagic shock, Myelofibrosis, Uveitis, Glaucoma, Blindness and/or vision impairment level, Retinal disorder,

disorders of the of cornea, Injury of eye region, Chronic fatigue syndrome, Anxiety disorder, Amnestic disorder, Autistic disorder, Schizophrenia, Psychotic disorder, dementia, mood disorder, cystic fibrosis, Severe combined immunodeficiency disease, Congenital chromosomal disease, Down syndrome, Anomaly of chromosome X, Myelodysplastic syndrome with isolated del(5q), Turner syndrome, Anomaly of chromosome pair 11, ataxia-telangiectasia syndrome, disorders of the pancreas, Diabetes mellitus, disorders of the thyroid gland, general adaptation syndrome, disorders of the endocrine system, Chronic renal impairment, conjunctiva, squamous cell carcinoma, basal cell carcinoma, basaloid tumor, breast tumor, colorectal cancer, lymphoma, B-cell lymphoma, corneal ulcer, colitis, Large cell carcinoma, prurigo (e.g., P. nodularis), sepsis, septicemia, cardiovascular inflammation, lymphedema, and fibrosis (including scar formation)

General

In preferred embodiments of the disclosed methods, treatments, medicaments, regimens, uses and kits, the IL-17 antagonist is an IL-17 binding molecule. In preferred embodiments, the IL-17 binding molecule is an IL-17 antibody or antigen-binding fragment thereof. In preferred embodiments of the disclosed methods, treatments, regimens, uses and kits, the IL-17 antibody or antigen-binding fragment thereof is a human antibody of the IgG_1 isotype. In preferred embodiments of the disclosed methods, the antibody or antigen-binding fragment thereof is Secukinumab, CJM112 or a functional derivatives or biosimilar thereof. In even more preferred embodiments of the disclosed methods, the antibody or antigen-binding fragment thereof is secukinumab or CJM112.

The details of one or more embodiments of the disclosure are set forth in the accompanying description above. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present disclosure, the preferred methods and materials are now described. Other features, objects, and advantages of the disclosure will be apparent from the description and from the claims. In the specification and the appended claims, the singular forms include plural referents unless the context clearly dictates otherwise. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. All patents and publications cited in this specification are incorporated by reference. The following

Examples are presented in order to more fully illustrate the preferred embodiments of the disclosure. These examples should in no way be construed as limiting the scope of the disclosed patient matter, as defined by the appended cl**EXAMPLES:**

Example 1: IL-17 Pathway Signature is Induced in Acne

Material and Methods

IL17A signaling signatures were created using various cell types stimulated with the named cytokine. Primary human juvenile foreskin keratinocytes were stimulated with IL17A (200ng/ml) or control for 18h, primary human juvenile foreskin fibroblasts stimulated with IL17A (200ng/ml) or control for 18h and dermatome sheets from human discard skin were stimulated with IL17A (1000ng/ml) or control for 18h. Samples were collected and processed for microarray analysis on Affymetrix HG_U133_Plus2 microarrays. RMA normalized samples were quality controlled, filtered for expressed genes.

IL17A signaling signatures were identified comparing stimulated and control groups with an unpaired T-test, identifying probesets with a corrected p-value below 0.05 and a fold change above 2.0.

The respective signature were used to calculate p-values with a Fisher's exact test which represent the statistical significance of observing an overlap between the signature and the 'disease gene list' (lesional vs non-lesional) of public datasets (Acne NCBI GEO identifiers GSE53795 and Psoriasis skin samples GSE13355).

Results and interpretation

As shown in **Figure 1**, IL17A signaling signatures created in skin or skin derived cell types using the cytokine as a stimulus show significant overlap to a disease gene list (lesional vs non-lesional) from a study with Acne patients, providing evidence that the IL17A pathway is active in this disease. As a confirmation and benchmark, a disease gene list from a psoriasis study was used. The p-values of the three different IL17A signaling signatures are comparable between the two different diseases. The detrimental role of IL17A in Psoriasis is well established and therefore we speculate that inhibiting the cytokine in Acne would be beneficial for the patient.

Example 2: IL-17A Production is Diminished by All-*Trans*-Retinoic Acid (ATRA) *in vitro*

Naive human peripheral blood CD4 positive T cells were purified by negative selection. Cells were cultured in the presence or absence of killed *Propionibacterium acnes* (*P. Acnes*). ATRA was added at the indicated concentrations (μM) and IL17A production by T cells was assessed by enzyme linked immunosorbent assay (ELISA).

P.Acnes induced IL17A production indicative of Th17 polarization in Donor 1 (**Fig. 2A**) and Donor 2 (**Fig. 2B**), while no detectable IL17 production was observed without P. acnes stimulation ("cont."). *P.acnes* induced IL17A production was suppressed by ATRA at all concentrations tested.

P. acnes is found in acne, and IL17A expressing T cells are also located in acne lesions. It is thus possible that ATRA exerts its antiinflammtory effect, in part, by suppression of Th17 cell priming. We conclude that reduced Th17 priming is likely to reduce inflammation in acne lesions and that an IL-17A antagonist, e.g., CJM112, may find use in treateing acne by reducing IL-17A signal and activity.

Example 3: A randomized, subject and investigator blinded, placebo-controlled, multi-center study in parallel groups to assess the efficacy and safety of CJM112 in patients with moderate to severe inflammatory acne

Purpose and rationale	The study is designed primarily to assess preliminary efficacy and safety of CJM112 in patients with moderate to severe inflammatory acne and to determine if CJM112 has an adequate clinical profile for further clinical development. In addition, sustainability of response and dose relationship will be explored.
Primary Objective	To assess the efficacy of CJM112 versus placebo on facial inflammatory lesion counts in patients with moderate to severe inflammatory acne
Secondary Objectives	To assess the safety and tolerability of CJM112 in patients with moderate to severe inflammatory acne To assess the pharmacokinetics of CJM112 in patients with moderate to severe acne
Study design	This is a randomized, placebo controlled, subject and investigator blinded, multicenter, non-confirmatory, parallel group, proof of concept study in patients with moderate to severe inflammatory acne. After an initial screening period (up to four weeks), the study is conducted in two consecutive treatment periods, each of 12 weeks, to show clinical efficacy and potential sustainability of response. Exposure to placebo will be limited to a maximum of 12 weeks. Patients are randomized to one of 3 treatment sequences (sequence 1, 2 or 3): 1 Patients randomized to treatment sequence 1 will receive active treatment (300 mg CJM112) throughout the study (both treatment periods) in monthly

	intervals, 2 Patients randomized to treatment sequence 2 will receive active treatment (75 mg CJM112) throughout the study (both treatment periods) in monthly intervals, 3 Patients randomized to treatment sequence 3 will receive placebo in treatment period 1 (up to 12 week) and at 12 weeks will receive a single dose of 300 mg CJM112 followed by monthly placebo treatment for treatment period 2. After the end of treatment period 2, all patients will be followed for safety and potential sustainability of efficacy, for an additional 12 weeks without any treatment. All patients will receive active treatment at some time in the study. The patients in sequence 1 receive a high dose monthly (300 mg s.c.). Patients in sequence 2 will receive a monthly dose of 75 mg s.c. All patients treated with placebo (sequence 3) will, after a period of 12 weeks, receive a single s.c. dose of 300 mg CJM112 followed by monthly s.c. injections with placebo.
Population	The patients included in the study are patients with moderate to severe inflammatory acne with not more than 5 nodules to exclude severe cases of nodulocystic acne, often associated with a high potential for scarring. A minimal count of 25 facial inflammatory lesions (papules, pustules, nodules) is needed for inclusion.
Key Inclusion criteria	• Written informed consent must be obtained before any assessment is performed. • Male and female subjects aged 16 to 45 years of age included, and otherwise in good health as determined by medical history, physical examination, vital signs, ECGs and laboratory tests. • Body weight between 50 and 120 kg, inclusive. • Papulo-pustular acne vulgaris having between 25 and 100 facial inflammatory lesions (papules, pustules and nodules), and presence of non-inflammatory lesions (open and closed comedones) on the face. • No more than 5 facial inflammatory nodules. • Investigator's Global assessment (IGA) score of at least moderate (3) acne severity. • Able to communicate well with the investigator, to understand and comply with the requirements of the study.
Key Exclusion criteria	• Use of investigational drugs at the time of screening, or within 4 weeks or 5 half-lives of screening, whichever is longer; or longer if required by local regulations. • Use of any topical anti-acne prescription treatment within 2 weeks and any OTC anti-acne treatment within 1 week of baseline (use of medicated (anti-acne) creams, medicated cleansers or medicated soaps is prohibited for the duration of the study). • Use of any oral/systemic treatment for acne, including oral antibiotics, dapsone, within 4 weeks prior to baseline. • Use of systemic or lesional injected (for acne) corticosteroids or systemic immunomodulators (such as cyclosporine, methotrexate, azathioprine, etc.) within 4 weeks before baseline. • Use of any systemic hormonal treatment (in particular anti-androgens, such as spironolactone, finasteride and cyproterone acetate) within 1 month before baseline. o Oral contraceptives can be continued if stable for the last 3 months before baseline if stable in dose and dosing regimen and type (brand) and if the patient plans to continue throughout the study period. • Previous treatment with biologics (such as anti-TNFα agents or anti-IL-1) within 3

	months prior to baseline; Anti-IL-12/23 blocking agents (such as briakinumab and ustekinumab or p19 antibodies) within 6 months prior to baseline. • Any previous treatment with IL-17 or IL17R blocking agents, including, but not limited to secukinumab, ixekizumab or brodalumab. • Use of oral retinoids (in particular isotretinoin) within the last 6 months prior to baseline. • Previous surgical, physical (such as ThermaClear™), light (including blue or UV light, photodynamic therapy [PDT]) or laser therapy within 4 weeks prior to baseline. After baseline, use of any tanning device, or excessive exposure to sun [with intention to tan], any handheld light device to treat skin or procedures for hair removal in the evaluated areas (face, neck and trunk) are not permitted. • Use of facial medium depth chemical peels (excluding home regimens) within 3 months prior to baseline. • Any live vaccines (this includes nasal-spray flu vaccine) starting from 6 weeks before baseline • Any other forms of acne, such as: o Presence of cysts and severe nodulocystic acne, and any acne type with a high risk of severe scarring. o Secondary acne, including drug induced acne. o Acne associated with known hormonal imbalances such as polycystic ovaries, Cushing syndrome, congenital adrenal hyperplasia (CAH), etc. o Acne as part of a known genetic syndrome. o Extensive (acne) keloids and hypertrophic scarring making clinical evaluation difficult. o Hidradenitis suppurativa, also called Acne inversa. o Other forms of acne rosacea, peri-oral dermatitis and gram-negative folliculitis. • History of severe systemic Candida infections or evidence of Candidiasis in the 2 weeks prior to baseline. • At screening, history or symptoms of malignancy of any organ system Evidence of active tuberculosis at screening. • Patients with known active Crohn's disease • History of immunodeficiency diseases (positive Hepatitis B surface antigen or Hepatitis C test result at screening) • Pregnant or nursing (lactating) women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive human chorionic gonadotropin (hCG) laboratory test. • Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective methods of contraception during dosing and for 13 weeks after stopping medication.
Study treatment	Treatment sequence 1: Period 1 (12 weeks): CJM112 high dose (300 mg) monthly Period 2 (12 weeks): CJM112 high dose (300 mg) monthly Treatment sequence 2: Period 1 (12 weeks): CJM112 low dose (75 mg) monthly Period 2 (12 weeks): CJM112 low dose (75 mg) monthly Treatment sequence 3: Period 1 (12 weeks): Placebo monthly

	Period 2 (12 weeks): one active single dose CJM112 high dose (300 mg), followed by placebo monthly
Efficacy/PD assessments	• Global acne assessment such as Investigator Global Assessment (IGA) for facial acne assessments and Comprehensive Acne Severity Scale (CASS) for non-facial assessments • Lesion counts (inflammatory, non-inflammatory, nodules) • Patient-Reported Outcomes (PRO) such as the dermatology Life quality index [DLQI], patient global assessment, Patient's satisfaction questionnaire) • Exploratory biomarkers (blood, skin biopsies, and sebum)
Key safety assessments	• AE monitoring • Physical examinations • Monitoring of laboratory markers in blood and urine • ECG • Vital signs
Other assessments	• Digital photography (selected centers)
Data analysis	The log transformed inflammatory facial lesion count will be analyzed using a mixed effect model for repeated measures (MMRM), with log transformed baseline inflammatory facial lesion count as a covariate; treatment group, visit, treatment group by visit interaction and log transformed baseline inflammatory facial lesion count by visit interaction as fixed effects and subject as a random effect. The results will be reported in terms of ratio of geometric means.

CJM112 in monthly injections was tested in an ongoing double blind, randomized, multi-center, placebo controlled study with moderate to severe inflammatory acne who failed systemic treatment and had at least 25 facial inflammatory lesions at inclusion. Based on 12-week data from the first 9 patients, at week 12 after three injections, facial inflammatory lesions (sum of papules and pustules and nodules) show a clinically significant reduction from baseline reaching 63% for CJM112 (n=5), while placebo reached 35% (n=4). In one CJM112 treated patient, the total facial inflammatory lesion count went down from 33 to 1 after 24 weeks treatment, which may corresponds to a near clearance status. Nodules as a sign of a more severe disease were reduced only by CJM112 and not with placebo, which hints to a clinical activity in nodular or nodulocystic acne. The observed clinical efficacy in reducing inflammatory lesions is superior to what is observed with other systemic treatments such as antibiotics in placebo-controlled studies in somewhat less severe patients (where an efficacy of 46% from baseline was observed, *Fleischer 2006*). However, it compares well to treatment efficacy of isotretinoin, associated with several serious side effects, such as teratogenicity and suicidal ideation, even if not placebo

controlled (see *Lee 2011*, "Effectiveness of conventional, low-dose and intermittent oral isotretinoin in the treatment of acne: a randomized, controlled comparative study; british Journalof Dermatology; 164, pages 1369-1375, in particular the figure 4; or Fleischer et al "*Safety and efficacy of a new extended-release formulation of minocycline*", Cutis, pages 21-31, Volume 78, October 2006, in particular the figure on page 26).

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Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65                  70                  75                  80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
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Cys Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg Thr Val Ala
            100                 105                 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
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Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
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Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145                 150                 155                 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
                165                 170                 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
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Val Arg Asp Tyr Tyr Asp Ile Leu Thr Asp Tyr Tyr Ile His Tyr Trp
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Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Ala
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Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
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Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
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Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
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Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr

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Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
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Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
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Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
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Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
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Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                325                 330                 335

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            340                 345                 350

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
        355                 360                 365

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    370                 375                 380

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
385                 390                 395                 400

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                405                 410                 415
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50 55 60

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Tyr Asp Ala Ser Ser Leu Glu Gln Gly Val Pro Ser Arg Phe Ser Gly
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Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe Asn Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser

165 170 175

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Gly

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35 40 45

Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val
50 55 60

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Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
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            100                 105                 110

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            20                  25                  30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Arg Gly Ser Leu Tyr Tyr Trp Gly Gln Gly Thr Leu Val
            100                 105                 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
        115                 120                 125
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Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
    130                 135                 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145                 150                 155                 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
                165                 170                 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu
            180                 185                 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
        195                 200                 205

Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
    210                 215                 220

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
225                 230                 235                 240

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
                245                 250                 255

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
            260                 265                 270

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
        275                 280                 285

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
    290                 295                 300

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305                 310                 315                 320

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
                325                 330                 335

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
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            340                 345                 350

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
        355                 360                 365

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
    370                 375                 380

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
385                 390                 395                 400

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
                405                 410                 415

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
            420                 425                 430

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445
```

WHAT IS CLAIMED IS:

1. An IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne, e.g. moderate to severe acne, e.g. moderate to severe inflammatory acne.

2. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to claim 1, wherein the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of mature human IL-17: a) between residues Arg 55 and Trp 67; b) comprising residues Arg 55, Glu 57, and Trp 67; c) comprising residues Arg 55, Glu 57, Trp 67, Tyr 62, and Arg 101; d) comprising residues Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, and Val 65; or e) comprising residues Arg 55, Glu 57, Trp 67, Tyr 62, Arg 101, Pro 59, Ser 64, Val 65, Val 22*, Leu 26, Asp 58, Glu 60, Pro 63, Pro 107, Phe 110, and Lys 114*, where amino acids marked with (*) designate a residue contributed by the second IL-17 subunit of the IL-17A homodimer, and further wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 1-10 pM and an in vivo half-life of about 2-4 weeks, e.g., about 3 weeks.

3. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to claim 1, wherein the IL-17 antibody or antigen-binding fragment thereof binds to an epitope of a human IL-17 homodimer having two mature human IL-17 protein chains, said epitope comprising residues Leu74, Tyr85, His86, Met87, Asn88, Val124, Thr125, Pro126, Ile127, Val128, His129 on one chain and Tyr43, Tyr44, Arg46, Ala79, Asp80 on the other chain, wherein the IL-17 antibody or antigen-binding fragment thereof has a K_D for human IL-17 of about 100-200 pM, and wherein the IL-17 antibody or antigen-binding fragment thereof has an *in vivo* half-life of about 3-5 weeks, e.g., about 4 weeks.

4. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to claim 1 or 2, wherein the IL-17 antibody or antigen-binding fragment thereof

comprises:

i) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:30;

ii) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:22;

iii) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:30 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:22;

iv) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28;

v) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20;

vi) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27 and SEQ ID NO:29;

vii) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21;

viii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:24, SEQ ID NO:26, and SEQ ID NO:28 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:16, SEQ ID NO:18 and SEQ ID NO:20;

ix) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:25, SEQ ID NO:27, and SEQ ID NO:29 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21;

x) a light chain comprising SEQ ID NO:23; xi) a heavy chain comprising SEQ ID NO:31;

xii) a light chain comprising SEQ ID NO:23 and a heavy chain comprising SEQ ID NO:31; or

xiii) an immunoglobulin domain or chain comprising an amino acid sequence having at least about 90%, 95%, 98% or 99% overall sequence identity to the amino acid sequence hereinabove defined under i) to xii).

5. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing

acne according to claim 1 or 3, wherein the IL-17 antibody or antigen-binding fragment thereof comprises:

i) an immunoglobulin heavy chain variable domain (V_H) comprising the amino acid sequence set forth as SEQ ID NO:8;

ii) an immunoglobulin light chain variable domain (V_L) comprising the amino acid sequence set forth as SEQ ID NO:10;

iii) an immunoglobulin V_H domain comprising the amino acid sequence set forth as SEQ ID NO:8 and an immunoglobulin V_L domain comprising the amino acid sequence set forth as SEQ ID NO:10;

iv) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3;

v) an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6;

vi) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13;

vii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6;

viii) an immunoglobulin V_H domain comprising the hypervariable regions set forth as SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13 and an immunoglobulin V_L domain comprising the hypervariable regions set forth as SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6;

ix) an immunoglobulin light chain comprising the amino acid sequence set forth as SEQ ID NO:14;

x) an immunoglobulin heavy chain comprising the amino acid sequence set forth as SEQ ID NO:15;

xi) an immunoglobulin light chain comprising the amino acid sequence set forth as SEQ ID NO:14 and an immunoglobulin heavy chain comprising the amino acid sequence set forth as SEQ ID NO:15; or

xii) an immunoglobulin domain or chain comprising an amino acid sequence having at

least about 90%, 95%, 98% or 99% overall sequence identity to the amino acid sequence hereinabove defined under i) to xi).

6. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any one of the claims above, wherein the IL-17 antibody or antigen-binding fragment thereof is a human antibody.

7. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any of the above claims, wherein the IL-17 antibody or antigen-binding fragment thereof is administered for up to 24 weeks.

8. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any the above claims, wherein the IL-17 antibody or antigen-binding fragment thereof is administered quarterly or monthly, e.g. subcutaneously at a dosing of about 75 mg to about 600 mg or about 75 mg to about 300 mg.

9. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to claim 8, wherein the IL-17 antibody or antigen-binding fragment thereof is administered, by subcutaneous injection, at an unit dose of about 75 mg, about 150 mg, about 300 mg, about 450 mg or about 600 mg.

10. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any of the above claims, wherein the IL-17 antibody or antigen-binding fragment thereof is administered by subcutaneous injection at an unit dose of about 75 mg to about 600 mg, preferably about 75 mg to about 300 mg, wherein said administering is not preceded by administering said IL-17 antibody or antigen-binding fragment in a loading regimen.

11. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to claim 9 or 10, wherein the unit dose is administered monthly or weekly.

12. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any of the above claims, wherein the IL-17 antibody or antigen-binding fragment thereof is administered by subcutaneous injection, weekly, at a loading dose of about 75 mg to about 600 mg, preferably about 75 mg to about 300 mg.

13. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to claim 12, wherein the loading dose is administered during 1 to 8 weeks, preferably during 4 or 5 weeks.

14. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to claim 13, wherein the IL-17 antibody or antigen-binding fragment thereof is administered subcutaneously at a dosing of about 75 mg to about 600 mg, preferably about 75 mg to about 300 mg, weekly during week 0, 1, 2, 3, and 4, and then monthly thereafter.

15. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any one of claims 1 to 6, wherein the IL-17 antibody or antigen-binding fragment thereof is administered as a single dose, e.g. of about 150 mg to about 600 mg subcutaneously.

16. An IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to claim 4 or any one of claims 6 to 15 , wherein the IL-17 antibody or antigen-binding fragment thereof is CJM112, a functional derivative thereof or a biosimilar thereof, e.g. CJM112,

17. An IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to claim 16, wherein the IL-17 antibody or antigen-binding fragment thereof is CJM112, a functional derivative thereof or a biosimilar thereof, e.g. CJM112, and is administered subcutaneously at an unit dose of about 150 mg to about 600 mg, e.g. about 300 mg to about 450 mg.

18. An IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any one of claims 5 to 15, wherein the IL-17 antibody or antigen-binding fragment thereof is secukinumab, a functional derivative thereof or a biosimilar thereof, e.g. Secukinumab.

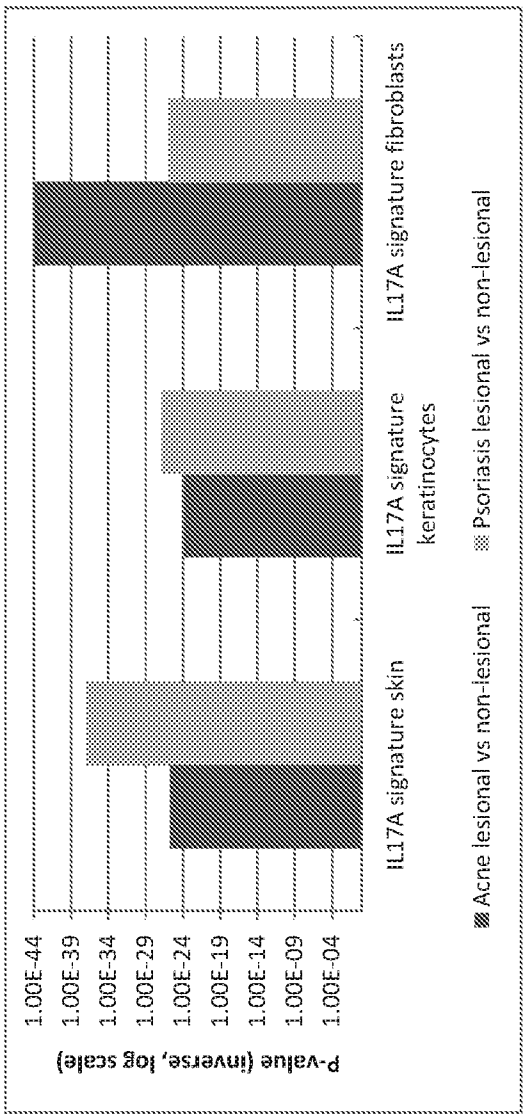
19. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing moderate to severe acne according to claim 18, comprising administering the patient a single dose of about 150 mg to about 600 mg of secukinumab, a functional derivative thereof or a biosimilar thereof, e.g. secukinumab, by subcutaneous injection.

19. An IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing moderate to severe acne, that is secukinumab, a functional derivative thereof or a biosimilar thereof, e.g. Secukinumab, wherein the IL-17 antibody or antigen-binding fragment thereof is administered subcutaneously at a dosing of about 75 mg to about 600 mg, preferably about 75 mg to about 300 mg, weekly during 1 to 8 weeks, and then monthly thereafter.

20. The IL-17 antibody or antigen-binding fragment thereof for use in treating or preventing acne according to any above claims, wherein the patient was previously treated for acne with a topical anti-acne treatment, an oral/systemic anti-acne treatment, a systemic or lesional injected anti-acne treatment, or surgical, physical, light or laser therapy.

.

FIG 1.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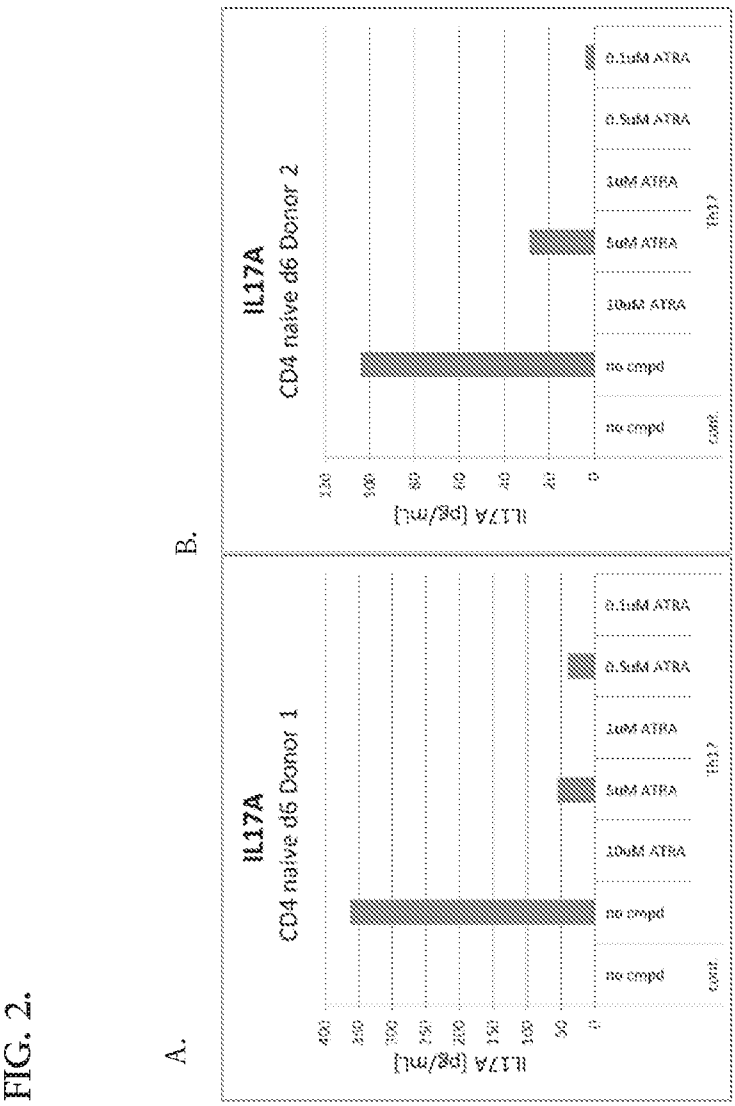
IL17A signature keratinocytes
IL17A signature fibroblasts
Acne lesional vs non-lesional
Psoriasis lesional vs non-lesional

FIG. 2.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0.5uM ATRA
1uM ATRA
5uM ATRA
10uM ATRA
no cmpd
no cmpd
ctrl
ATRA
B.
IL17A
CD4 naive d6 Donor 2
IL17A [pg/mL]
120
100
80
60
40
20
0
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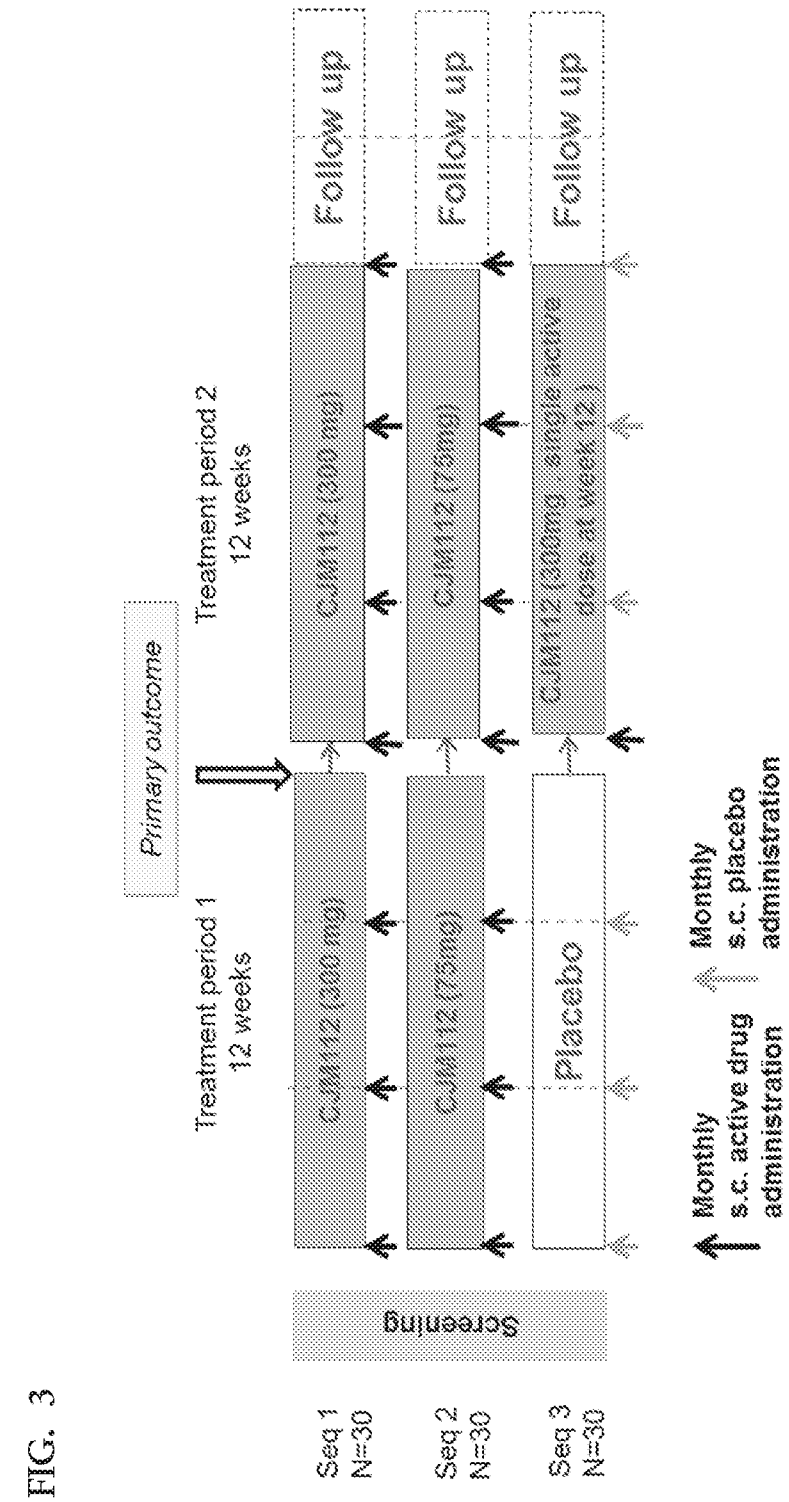
no cmpd
ctrl
ATRA

FIG. 3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Seq 2 N=30
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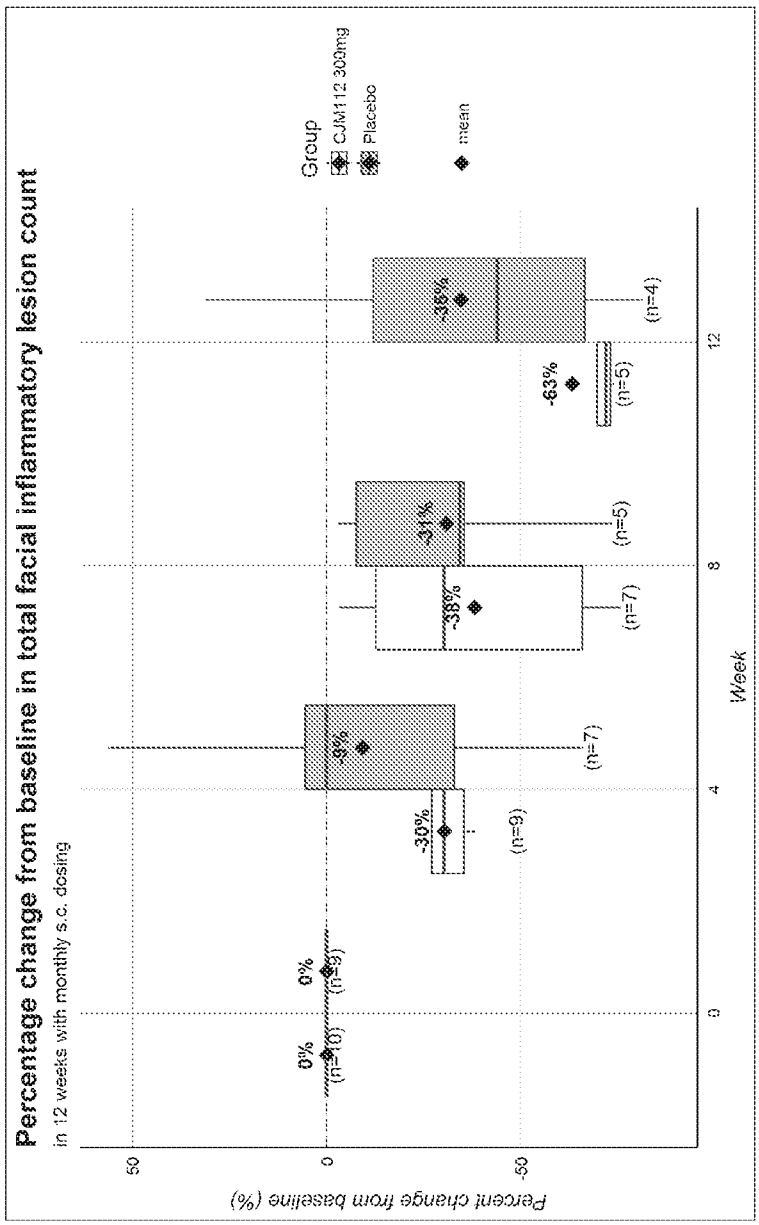
Treatment period 2 12 weeks
Primary outcome
Placebo
Follow up
Follow up
Follow up
Monthly s.c. active drug administration
Monthly s.c. placebo administration

FIG 4:


Percentage change from baseline in total facial inflammatory lesion count
in 12 weeks with monthly s.c. dosing
Group
CJM112 300mg
Placebo
mean
Percent change from baseline (%)
50
0
-50
0
4
8
12
Week
0%
0%
(n=10)
(n=9)
-9%
-30%
(n=7)
(n=9)
-38%
-31%
(n=7)
(n=5)
-63%
-35%
(n=5)
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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2017/057330

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K39/395 A61P17/10 C07K16/24
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	George Agak: "Silencing of IL-17 modulates inflammatory and antimicrobial defense responses mediated by Propionibacterium acnes", , 1 May 2014 (2014-05-01), XP055449356, Retrieved from the Internet: URL:http://www.jimmunol.org/content/192/1_Supplement/184.8 [retrieved on 2018-02-08] the whole document ----- -/--	1-20

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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Date of the actual completion of the international search	Date of mailing of the international search report
9 February 2018	13/03/2018

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Cilensek, Zoran

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